

SCIENCE

SEPTEMBER 15, 1950



SELF-AWARENESS AND
SCIENTIFIC METHOD

GEORGE F. F. LOMBARD

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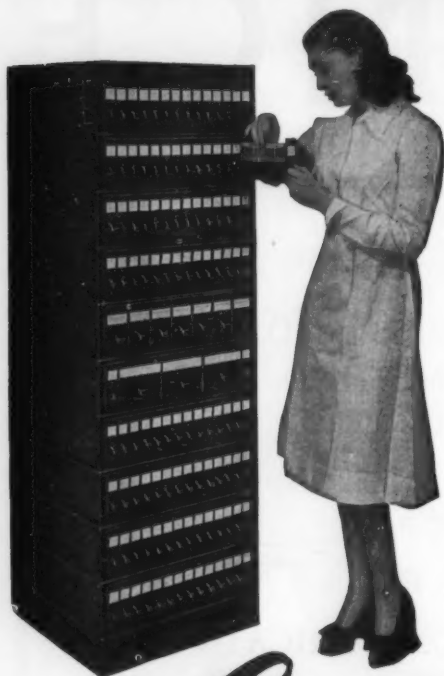
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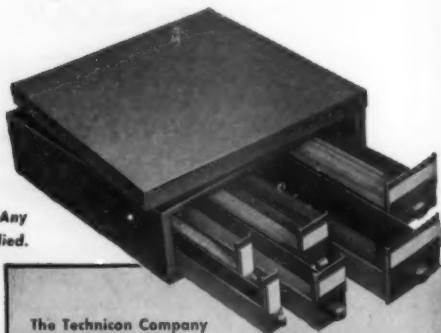
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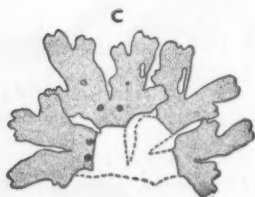
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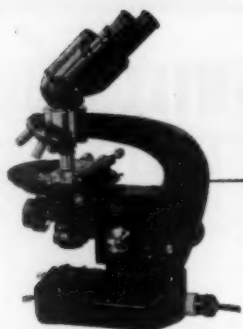
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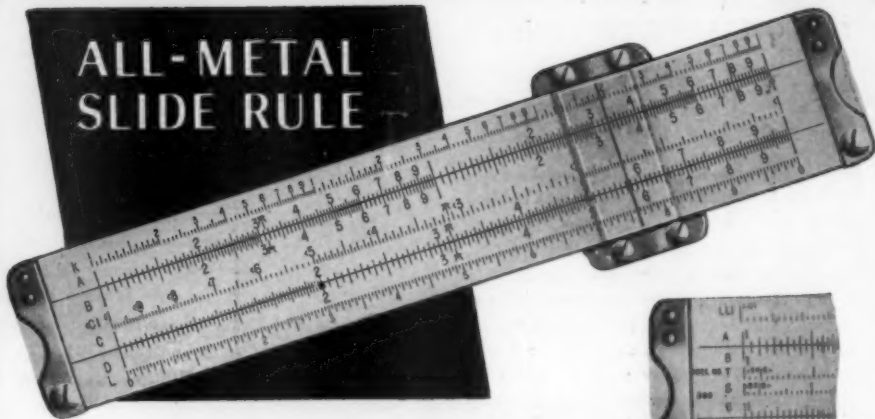
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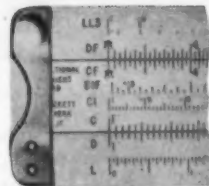
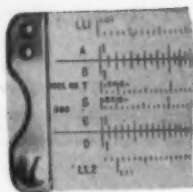
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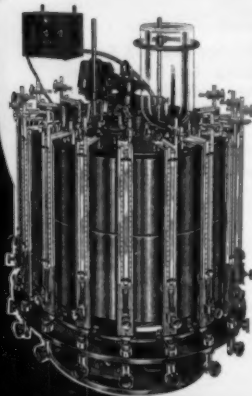
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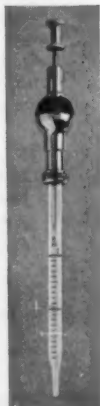
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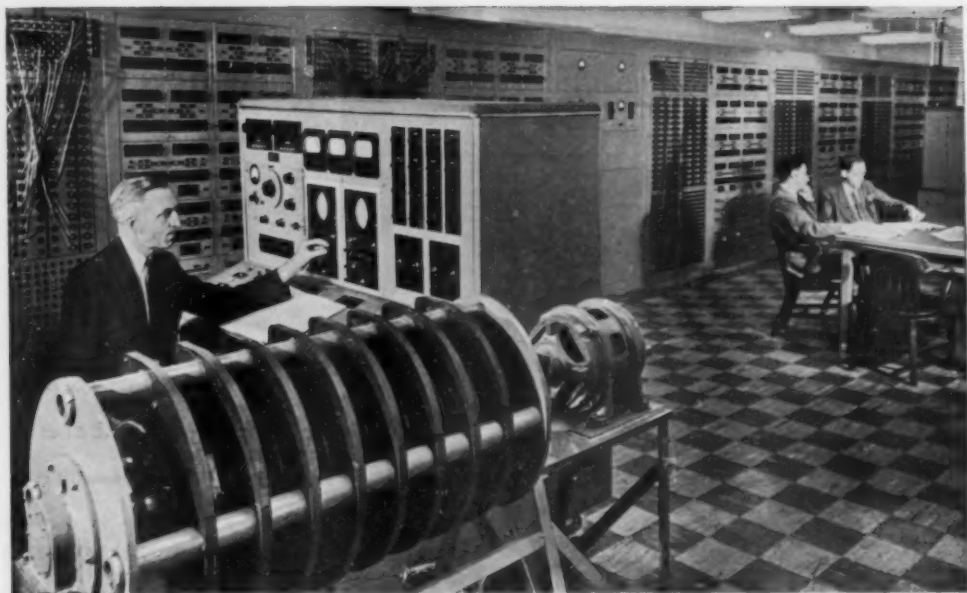
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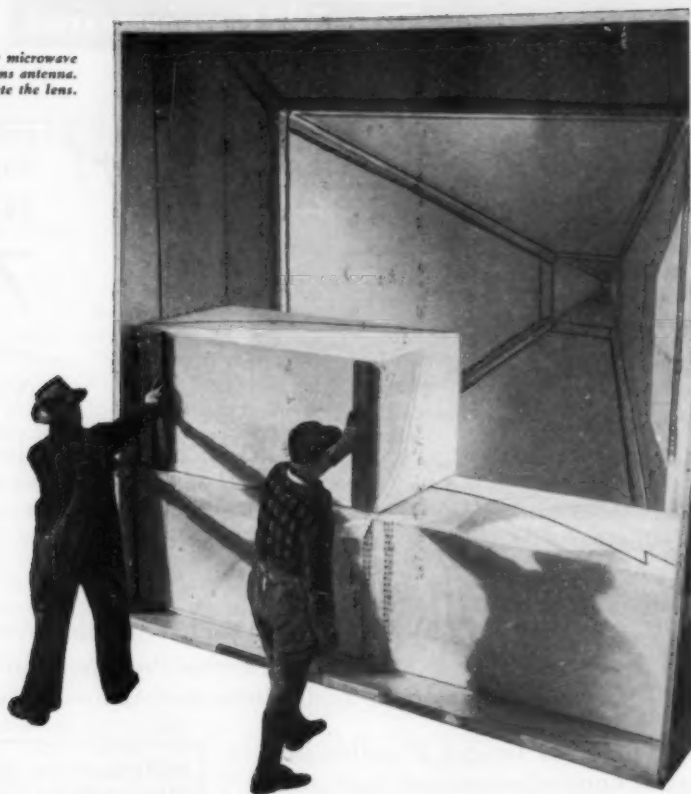
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Self-Awareness and Scientific Method¹

George F. F. Lombard

Graduate School of Business Administration, Harvard University, Boston, Massachusetts

THE RECENT SUCCESSES of the natural sciences have arisen from the use of controlled experiments. In teaching and research they receive primary attention. This is entirely appropriate to the needs and opportunities of those sciences: the whole history of controlled experiments in them has been that they are fruitful of new knowledge. Their history in the social sciences, with few exceptions, is that they have not. Since one man's meat is frequently another's poison, the techniques of the controlled experiment are not what I wish students of human behavior would learn from the natural sciences. My reasons for this reside in two familiar but neglected skills without which science has nowhere progressed.

I

Experiments may fail for many reasons: only those based on relevant observation of nature have any chance of fruitful results. Since before Galileo's "fantastically artificial" neglect of friction in his experiments with motion, the experiments of natural scientists have, on the whole, been relevant to the nature of things; the results of the polls taken before the 1948 elections are evidence that many in the social sciences have not.

Claude Bernard said, "The experimental idea is by no means arbitrary or purely imaginative; it must always have support in observed reality; that is to say, in nature."² This concept of experiment is quite different from one current in the social sciences today, namely, that the limit of experiment is the ingenuity of the experimenter. But how are scientists to know what is relevant to nature? The difficulties here are great, especially so because research itself may distort

the natural happening of events. How can that be studied which study itself distorts?

Natural scientists have long been aware of the problem posed by the relationship of the researcher to his data. To be sure, in some of the natural sciences the presence of a researcher does not greatly affect the phenomena being studied. In others the phenomena must be shielded from, for example, the heat or electricity of an investigator's body. In biology and physiology the problems are quite different and often complex, even in simple experiments. Here also, thanks to the work of such investigators as Bernard, Cannon, and others, many of the obstacles have been overcome.

In the social sciences, the sensitiveness of the phenomena being studied to the presence of an investigator is especially great. This sensitiveness of human life to interaction with other human beings is familiar to all of us, and not only in research. It is demonstrated in every relationship. To clarify the point, let me take extreme examples.

Restrictive controls, short of the extinction of life itself, produce in those controlled diverse reactions, in all of which may be recognized attempts of the self to maintain its integrity. This seems to be true of parental, educational, administrative, military, and governmental controls. For example, this aspect of human behavior continually plagues the administrator who seeks to initiate change. In research, too, what we seek to control again and again resists the investigator and in often subtle ways upsets his plans. So, for many years, experiments in industry with rest pauses for workers were inconclusive: sometimes production increased following their introduction; sometimes it did not. Investigators cursed "human nature" until the researchers at Hawthorne began to understand the nature of their relationship to the workers in the test room.³

Impressive though reactions to violation of integrity are in human life, the positive effects of a relationship

¹ Expanded from remarks made at a discussion entitled "What the Social Scientist Would Like His Students to Know About the Natural Sciences," at the Harvard Summer School Conference on "The Place of Science in General Education," July, 1949. For the ideas behind these remarks, I am indebted to F. J. Roethlisberger for clarifying for me the importance of observation in scientific method, and to C. I. Barnard for crystallizing the concept of self-awareness.

² Claude Bernard. *An Introduction to the Study of Experimental Medicine*. New York: Henry Schuman, 1927, p. 38.

³ F. J. Roethlisberger and W. J. Dickson. *Management and the Worker*. Cambridge: Harvard University Press, 1939, Chap. VIII.

with others can be even more startling. The capacities of human beings to respond to warmth and appreciation with adaptation and growth are tremendous, although these powers are often latent. An article by Vincent Sheean entitled "On Love," in the July, 1949, *Atlantic Monthly*, gives an instance in point. Philosophy, religion, medicine, several of the social sciences, practical men of affairs, and military leaders have all documented this phenomenon. Whether human beings welcome or resist a relationship, their active response to one is apparent. My point is that in the social sciences, as in all science, an investigator's skills in handling his relationship to his data are of great importance.

II

But, granted an investigator needs skills in relating himself to his data, he must still make relevant observations. Although some physical scientists have had truly exceptional capacity in this direction, they have seldom made explicit the processes by which they achieved their results. Often, I suspect, they are not aware that there have been processes. Often they don't have to be conscious of them: their work has progressed far enough so that frequently they can take for granted the observations of nature on which an experiment is based. "At some time and in some way not recorded,"⁴ is a fairly typical description of the origin of an observation that led to fruitful experiment.

Not all records of observation are this incomplete. President Conant refers to Galileo and a pump that "was once called to his attention" (p. 33), and to Galvani, the frog's legs, and two people who are identified only as "one of the persons who were present" and "another one who was there." The fact that such careful observers as Galileo and Galvani failed to record the particulars of the situation in which their first observations occurred is indicative of the point I wish to make. Who was the person "who was present" who noticed the movement of the frog's legs? Who was "another one" who noticed that a spark seemed to excite the action? What was the background of their thinking that made them mention these observations to Galvani as possibly significant? Particularly, what in Galvani's thinking led him to seize at once on their remarks with "incredible zeal and eagerness," even though he "at the time had something else in mind and was deep in thought"?⁵

⁴James B. Conant. *On Understanding Science*. New Haven: Yale University Press, 1947, p. 37.

⁵James B. Conant. *Op. cit.*, p. 67. Cannon, without quoting sources, gives a slightly different account of these incidents, in which the same failure to record precisely the original observations is apparent. (Walter B. Cannon. *The Way of an Investigator*. New York: Norton, 1945, p. 69.)

Would that all of us when deep in thought could thus turn our minds into fruitful channels.

More detailed instances of how relevant observations have occurred can readily be found in Mach, Poincaré, Bernard, and others who have documented the progress of science. Cannon's *The Way of an Investigator* supplies us with valuable material. We also know something of the observations that led to the development of penicillin and radar. In all this material three phrases are used over and over again: "an accidental observation," "a hunch," and "chance." These words make me curious. Just what do they mean?

Two possibilities occur at once. The words hardly seem adequate as descriptive of a *process of thought*. On the other hand, they may reflect an *attitude of mind* that glories in the obviously brilliant results of the controlled experiment, to the neglect of the skilled observation. It is as if this attitude were saying, "What could be less worthy of attention than an accident, a hunch, or chance?" The choice of these words signifies how little the process is thought to deserve attention—and how little it receives. "It happened once; it was accidental; it will not happen again." "We made the most we could of it; why pay more attention to it?" A hunch: "A small thing; random; inexplicable. Now, when we can control the variables . . ."

Webster lists fourteen meanings for the word "chance." The fourteenth is: "The fortuitous . . . element in . . . existence; that which happens . . . in connection with events to which it bears no necessary relation." The first meaning is, simply, "The happening of events; the way in which things befall." I call to your attention the contrast of connotations in the fortuitous, the unrelated, and the inexplicable, on the one hand, and the happening of events, nature, on the other. Priestley redefines chance as "the observation of events arising from unknown causes."⁶ "Chance," with causes unknown, is surely distinct from chance without cause.

Please note, my claim is not that fortune plays no role in observation. Indeed it does; but when we have said that, have we said all there is to say? To me it seems not, though what else there is, is both difficult and complex to describe.

Certainly a skill of observation is something much more than what is involved when I say, "I see you." You are visible reality—at least, I find it fruitful for many purposes to assume that you are. What I mean by the process of observation is much more complex. To observe things in this other sense involves a way of thinking about things, as well as the data that are

⁶James B. Conant. *The Growth of the Experimental Sciences*. Cambridge: Harvard University Press, 1940, p. 53.

observed. Two psychologists, Snygg and Combs, have recently stated the dual nature of the process as follows:

The progress of science . . . is in two directions. The first is toward the discovery of new facts. This unceasing search is continually turning up new facts inexplicable in the old frames of reference. In turn, the scientist is forced to develop new frames of reference. Once a more adequate frame of reference has been achieved, its effectiveness is soon demonstrated by the discovery of a great number of new facts and relations.⁷

A skill of observation is, then, a capacity to discriminate between reality as it actually is and reality as any one of us sees it, determined as it is for us by the frames of reference, the conceptual schemes, which we habitually use. Some psychologists speak of this difference as the difference between "reality" and "perceived reality." To learn to step outside the conceptual schemes one habitually uses in search of new and more fruitful ones is no mean accomplishment. Science and philosophy have long pondered the problem.

III

President Conant's book *On Understanding Science* is helpful in giving us examples of the difficulties in the way of this learning process. Swammerdam, who experimented with frogs' legs but failed to push the work as Galvani did; Rey, whose work on calcination of tin should have exposed the phlogiston theory of combustion; the need of a new concept to "fit the times" if it is to be useful; and the "power of an old concept" to prevail against contradictory evidence are all to the point. President Conant says, "The history of science . . . fails to demonstrate any uniform way in which new experimental facts and observations generate the fruitful notions in the minds of great investigators" (p. 17).

Bernard has this to say: "Apropos of a given observation, no rules can be given for bringing to birth in the brain a correct and fruitful idea that may be a sort of intuitive anticipation of successful research" (p. 33).

These difficulties sound ominous for my purpose, but they give us a clue, for our question need not be the rules for getting from a given observation to an experimental idea. Our question can be, rather, "Are there any conditions of the mind which seem to assist the making of new observations?"

Bernard discusses at some length "a few general principles for the guidance of minds applying themselves to research (in experimental medicine)." Cannon, among others, speaks of "hard labor" (p.

67) and "the prepared mind" (p. 79). Both Conant and Cannon quote Pasteur, "Chance favors the prepared mind." Henderson's statement of the "conditions [necessary] for understanding" is well known: "first, intimate, habitual, intuitive familiarity with things; secondly, systematic knowledge of things; and thirdly, an effective way of thinking about things."⁸ His more precise description of "systematic knowledge" is by no means as familiar: "*Accurate observation of things and events, selection, guided by judgment born of familiarity and experience, of the salient and recurrent phenomena, and their classification and methodical exploitation*" [italics mine].⁹

Henderson's remarks describe usefully—at least, as he was wont to say, "to a first approximation"—the outward organization of training necessary to prepare a mind for fruitful observation. Since it is in the mind that an idea is generated, the process of creating one has an inner aspect as well. These outward conditions will not be productive unless they stimulate the growth of this inner capacity. A key to the ability to observe the difference between reality and reality as our existing conceptual schemes permit us to perceive it is awareness of our own frames of reference. If we know what they are, we are in a position to distinguish between them and reality. We can "see" that the world is round, not flat; that weights and feathers fall uniformly; that not all unions are "bad," and all managements "good," or vice versa.

In many of us, awareness of this sort remains low; in others it develops into an overriding—sometimes neurotic—conviction of sin that leads to crises of indecision and inaction. In still others, it achieves a balance that permits effective discrimination between reality and what we see as reality.

At this point I am faced with a difficult choice. The strict logic of my topic requires that I should describe as precisely as possible just what is the balance in the processes of the mind that leads to effective awareness. To do so would take me far into several theories of psychology, from which we would emerge convinced that the "gaps" in what is now known are more important than the "blocks" of what is known. Consequently, I propose to leap this hurdle by calling attention to two aspects of it: first, that the gap is there, and, second, that I am neglecting it.

Let me say only that a new idea worthy of attention seems always to spring from reflection. Consequently, balanced awareness involves an effective alternation between reflective thinking and concentrated attention. This fact is important in linking the general conditions of training of which I have been speaking with this

⁷ L. J. Henderson. *Sociology 23, Introductory Lectures*, Harvard University. Rev. October, 1938, p. 6. Mimeographed.

⁹ L. J. Henderson. "The Study of Man." *Science*, 1941, 94, 1.

⁷ Donald Snygg and A. W. Combs. *Individual Behavior*. New York: Harper, 1949, p. 5.

inner process of mind; for it follows that training must supply adequate material—that is, experience—for reflection, as well as an opportunity for the two kinds of thinking to develop in effective alternation with each other. The conditions Henderson laid down meet these requirements; but it is precisely at this point that we need to know much more about what learning is, and what the conditions are that favor it.

Let me repeat, the difficulty of acquiring an awareness of one's own frames of reference is great. It is especially so in the social sciences, where the investigator's own frames of reference, from which he draws the meaningfulness of his whole life, are called into question. Difficult and even painful as this learning process may be, it is nonetheless inevitable in the accumulation of knowledge; else the researcher fails to separate what he brings to the situation from the data he is studying.

IV

Skills in handling our relationship to the data we seek to study and skills in making relevant observations are related. Both require the inner quality of awareness of self of which I have been speaking. On the one hand, awareness of self increases our capacity for handling ourselves in relation to our data by forcing on us continuous and critical inner appraisal and reappraisal of what we are doing in relation to an external reality. On the other hand, it reinforces our capacity for accurate observation by making us conscious of the difference between that which we see (perceived reality) and reality. This awareness is as necessary in the training of social scientists as it is in general education for citizenship.

In the social sciences we often proceed as though we were unaware of the existence of the need. Our attempts to meet it have until recently been in one of two directions, both relatively sterile compared with progress in other sciences. On the one hand, we study situations far removed from what is familiar to us because we hope that the gross determinants of the behavior occurring in them will persist and be obvious to the investigator in spite of his presence. Studies of primitive tribes and cultures and of other groups at the fringe of our civilization have taken this direction. These studies are eminently worth while in their own right, and much of general value has been learned from them. Yet their methods leave us with a sense of something missing when we focus them on the problems of modern life. Too often, sensing "the shadow but not the substance" of our relationship to our data, we retreat into a pseudo-objectivity that defeats itself. By attempting to make our questionnaires, tests, and laboratory-type experiments completely objective, we arrive at a typical norm so far removed from the uniqueness of the particular in-

stance that the knowledge gained is all but useless in application.

Why I believe the quality of awareness is necessary in the training of a social scientist will, I hope, be clear by now. That quality in him is the seed from which new understandings of the way things happen will grow.

I believe this quality is equally needed today in general education in training for citizenship. When a boy-girl relationship becomes that of husband and wife, a couple cannot assume that communication between them over mutually created problems of children, housekeeping, and career will be eased by the understanding that arises from a common background. Indeed, most of us sooner or later have to realize that no such community of background exists. Under these conditions understanding, if it is to be achieved, must be demonstrated in face-to-face interactions in the present. This means that each of us must be able to recognize and behave in terms of what is important in our relationships here and now. Distinguishing this present reality from the way in which our past experiences have taught us to see it is vital to securing, first, understanding; then, communication and active cooperation.

Difficulties of communication between people exist not only in family relationships. They are a common symptom of our times. In industry they exist at every level of organization, between worker and worker, between foreman and worker, between staff specialist and line executive. They are particularly important and difficult between representatives of different organizations—business and government, business and labor, labor and government, government and government.

Let me take brief examples from foreign affairs; the needs are only less dramatic, hardly less acute, in the domestic economy. An administrator of the Economic Cooperation Administration interested in improving the efficiency of manufacturing in Europe, or a nutrition expert of the United Nations Food and Agricultural Organization seeking to improve the diet of southeast Asia, must each be aware of the threat to existing customs that his methods present. Without this awareness, what he is doing will inevitably seem to be destroying established ways of doing things, rather than creating new freedoms. His relationship and the relationship of our country to those peoples then come to be hated and feared, instead of becoming relationships through which they can seek the help to help themselves.

Administrative skills in instances such as these go a long way toward making good intentions effective, but they are never wholly so without understanding and support in the wider community. Indeed, now

that destruction for one may mean destruction for all, whole nations are called on for an awareness of self in relation to others such as has never before been required. At these levels the problems are of an entirely different order than any I have discussed up to this point. Yet, in peace and in war, citizen awareness of the effects of national policy is imperative. For example, however disastrous bombing may be to lives and property, it may also arouse to action a will to resist. The stubborn "happening of events" will then bring it about that this living resistance will replace both lives and property. If this should happen, bombing becomes a boomerang of a kind no primitive ever wished to possess. Even the *threat* of bombing may arouse such resistance.

And the threat is today a reality in the lives of all of us. Surely general education's responsibility to address the problems of communication between peoples cannot neglect these aspects of understanding: understanding of how what I myself do, of how what we as a nation do, affects and is affected by, the social realities of the divided world in which we live.

Many noted students of the social scene—Toynbee, Fromm, Rogers, Liebman, Whitehead—point to something closely akin to what I have been calling a conscious awareness of self in relation to the external world, as the chief need of civilization today. Our ignorance of what is required at these more complex levels is appalling; yet conditions today make it necessary to face the problems of research and education that are involved.

V

At the simpler levels, useful leads for organizing training in awareness are available, though neglected. One does not need to be a skilled observer to recognize that education does an uneven job in providing would-be researchers and citizens with foundations for the development of these skills.

In both school and college the emphasis is on systems of knowledge, a quite different thing from "systematic knowledge." Our conceptual schemes are more often "theories of explanation"¹⁰ than fruitful ways of helping us to new observations. We leave the acquisition of "intuitive familiarity" to chance, or neglect it entirely, in spite of good examples set us in engineering, and especially in medicine.

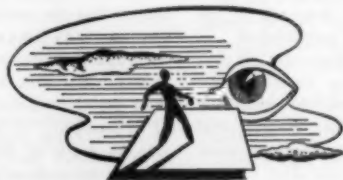
¹⁰ L. J. Henderson. *Op. cit.*, pp. 8-10.

Beyond this, experience suggests that training organized under the burden of responsibility in connection with the handling of actual situations provides a favorable climate for self-awareness to mature into active skill. Henderson makes much of this point and refers both to medical training and to what I believe was once known as "Milner's Kindergarten" as a case in point in a quite different field, that of government administration.¹¹ Yet, everywhere in education, especially in the training of ourselves, the teachers, neglect and chance have captured the "burden of responsibility."

I could mention "self-directive" interviewing as a promising new tool of research for some fields of the social sciences. The recent suggestion of an "internal frame of reference" as an appropriate conceptual scheme for psychology may be most fruitful. Role-playing and several forms of group discussion, such as group therapy and group dynamics, are having some success in developing effective self-awareness. Semantics and psychoanalysis also have important contributions, as may the psychodrama and sociodrama. I would be overly self-aware indeed if I did not mention, too, our rather different use of case method instruction in human relations in General Education at Harvard College and in the Graduate School of Business Administration. We have plans for new, as yet untried, ways of training in social skills under the burden of responsibility.

I have now tried—I am sure, inadequately—to clarify two aspects of scientific method, the importance of which I wish students of human behavior could learn from the natural sciences. I have described them as skills of handling oneself in relation to one's data and as skills of making relevant observations of nature. An inner quality of the mind, which I have called self-awareness, seems to me a key to their acquisition. At this stage of the growth of knowledge in the social sciences, I give techniques of experimentation secondary emphasis. As social scientists learn to handle their relations with their data and to make relevant observations, I am confident that experimentation will reappear in ways that do not distort the happening of events. Our start is to learn to make accurate observations of nature.

¹¹ See also John Buchan. *Pilgrim's Way*. Boston: Houghton Mifflin, 1940, pp. 100 ff.



Clifford Dobell, F.R.S.: 1886—1949

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THE DEATH of Clifford Dobell on December 23, 1949, following a cerebral hemorrhage two weeks previously, removed one of the leading protozoologists of our time. A man of indefatigable industry, of remarkable clarity of observation, of extreme independence of thought, and of a refreshing individuality of style in his published writing, Dobell exerted a strong influence in many fields of protozoology. A student at Sedgwick at Cambridge, and later of Richard Hertwig at Munich, his earliest important work was the treatise *The Principles of Protistology*, which he published at the age of 25. In this paper he suggested important concepts to be developed in the later growth of the science of protozoology—for example, the view that protozoa are not homologous with single cells of multicellular organisms, but might be considered to be noncellular, as well as the argument that protozoa are in no sense simple or primitive organisms.

During World War I, Dr. Dobell served as a director of training for the British War Office in identifying human intestinal protozoa. This led to a study of the intestinal protozoa, especially of the endamebae of man. His pioneer researches on these organisms culminated in the publication of *The Amoebae Living in Man*, in 1919, and *The Intestinal Protozoa of Man*, with F. W. O'Connor, two years later. These are still classics in their fields.

From these investigations he entered upon still another phase, perhaps the most fruitful of all: the working out of the complete life histories of the intestinal amebae of man and monkey *in vitro*. He was the first to follow the complete life history in culture of *Endameba histolytica*. He demonstrated the cross-infection of all the amebae of man for macaques and of the similar forms in the monkey for man. In this work Dobell used himself as the human test animal and succeeded in infecting himself with practically all the intestinal amebae and flagellates of man. This was followed by a study of the behavior of these intestinal protozoa under different cultural conditions. The experimental phases were brought to a close only shortly before he retired as protistologist at the National Institute for Medical Research in the fall of 1949, and the results are largely unpublished.

In 1915 Dobell and A. P. Jameson demonstrated that zygotic meiosis, with an accompanying haploid cycle, occurs in the coccidian *Aggregata* and the gregarine *Diplocystis*. This proved to be another fundamental contribution to protozoology in which he played a most important part.

In 1908 he spent some months at the Zoological Station at Naples. From work done at this time came, among other papers, the meticulous and now-classical life history of the coccidian *Aggregata* in the cuttlefish and the crab.

Probably Dobell's magnum opus, and the work for which he is best known beyond the field of protozoology, is the magnificent biography *Antony van Leeuwenhoek and his "Little Animals,"* which was published in 1932. This labor of love was begun by Dobell before World War I; part of it was written during the zeppelin raids on London. To write it Dobell taught himself, first, modern Dutch and then seventeenth-century Dutch, after he discovered that Leeuwenhoek's *Letters* to the Royal Society were not otherwise decipherable. One of the last papers published during Dobell's lifetime was his biography of D'Arcy W. Thompson, in the *Obituary Notices of Fellows of the Royal Society* for November, 1949. It was to D'Arcy Thompson, "my oldest and greatest friend," said Dobell, that he had dedicated in part the *Antony van Leeuwenhoek* with the words *Fratri carissimo D'Arcy Wentworth Thompson Scoto haec acta mortui batavi D.D.D. Editor Anglus animalculum Elephanti*.

Personally, Dobell was a prodigious and a meticulous worker, who insisted on carrying out every observation and making every preparation or examination himself. He abhorred the present-day practice of "research teams" and, during his thirty years at the National Institute for Medical Research, he consistently refused to accept the opportunity to employ research assistants. He wrote in a trenchant yet engaging style, and his published writings abound with footnotes that bring an added zest to an already vital page. His very honesty and sincerity militated against the use of "diplomatic" language or the glossing-over of what he considered to be shoddy scientific work. If he thought a man's experiments to be inadequate, or his conclusions invalid, Dobell did not hesitate to point this out in so many words. The result was a strong resentment on the part of some of those criticized and a feeling that Dobell had little respect for the work of others. Actually, he was more generous with his praise for work well done than he was with his criticism of what he believed had been done poorly. His first love was science, and his judgments were based on accuracy of observation and carefulness of experiment. It will be only rarely that anyone who was as much of an individual as Clifford Dobell can develop again in science in the near future.

Technical Papers

The Influence of ACTH and Cortisone on Certain Factors of Blood Coagulation

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In both experimental animals and in man a variety of factors has been observed to induce changes in the coagulability of blood. Cannon (2) demonstrated that epinephrine, when injected into the experimental animal in small amounts, accelerates clotting, whereas in a large amount it materially delays coagulation. Moon (9), Eagle *et al.* (4), Howell (6), and Jacques and Waters (7) have ascribed the prolonged clotting time of shock to a circulating antithrombin. Evidence that the anticoagulant in anaphylactic shock is heparin has been presented by Jacques (7) and Jorpes *et al.* (8), who hold that it is released from the mast cells. More recently, Dougherty and Dougherty (5) have shown similar changes in the mast cells of the experimental animal receiving 11-dehydro-17-hydroxycorticosterone (cortisone). Selye (12) has stated that the "alarm reaction," in general, decreases the clotting time and has postulated that the frequent occurrence of thrombosis following injuries or surgical procedures may be related to humoral factors released in response to stress. In man, disease with inflammation, necrosis, and thrombosis have each been shown by Schilling and DeNatale (11) to be accompanied by significant changes in the prothrombin times, which are not necessarily reflections of altered heparin levels.

In the light of these observations and on the premise that exogenous adrenocorticotrophic hormone (ACTH) induces some changes in the human being that qualitatively simulate the response to stress, it appeared desirable to determine what effect this hormone and cortisone might have on the coagulation mechanism. To date, observations during hormonal therapy have been made on 20 patients receiving ACTH¹ and on 6 receiving cortisone² for the experimental treatment of ocular and certain collagen diseases. In addition, selected control studies have been made on 3 patients with Addison's disease, on 1 with hypopituitarism, on 1 individual with fatigue and diarrhea, and on 3 normal persons.

¹ Obtained from the Armour Laboratories, Chicago, through the cooperation of John R. Mote, medical director.

² Obtained from the Merck Laboratories, Rahway, N. J., through the courtesy of J. M. Carlisle, medical director.

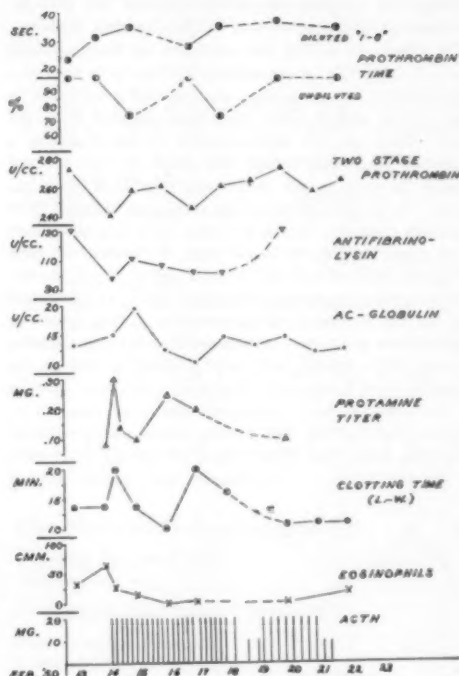


FIG. 1.

The following blood studies were made: clotting times by modified Lee-White and/or Howell procedures; direct platelet counts using the Rees-Ecker solution; undiluted prothrombin times³ according to Quick (10); "1 to 3" plasma-diluted prothrombin times³ by the Link-Shapiro method (13); heparin or heparinlike levels by a modification of the protamine titration of Allen (1); direct eosinophil counts by a modified Forsham-Thorn technique (6); and plasma accelerator (ac) globulin, antifibrinolytic, and two-stage prothrombin levels, as determined in the laboratory of W. Seegers,⁴ of Wayne University College of Medicine, Detroit.

In the 3 normal persons used as controls, a single 20-mg intramuscular injection of ACTH produced in 4 hr a significant increase in circulating heparin or heparinlike material, a parallel prolongation of the clotting time,

³ We are indebted to F. W. Hartman and V. Schelling, of the Division of Laboratories, Henry Ford Hospital, for these determinations.

⁴ We express our thanks to Dr. Seegers for his generous help in these studies.

and the usual reduction in the circulating eosinophils.

These changes are represented on the left side, lower portion of Fig. 1, following the initial 20-mg injection of ACTH in this normal male. In the 2 normals receiving only one dose of ACTH, a return to the control levels was noted by the 8th hr. In the one (Fig. 1) who continued to receive 20 mg every 4 hr, the protamine titer and clotting time had reached control levels by the 20th hr, and the eosinophil count continued the expected decline.

The effects of ACTH and cortisone on blood clotting time and on certain of the constituents known to be active in the coagulation mechanism are depicted graphically in Figs. 1, 2, 3, and 4, which have been selected from the series. They are not representative of the group as a whole but illustrate, rather, the scope of the induced changes, as well as the differences that have been observed. In general, there are no consistent changes from patient to patient. The alterations following these hormonal agents appear to be, in part, a function of both the initial level of adrenal cortical activity and the integrity of the coagulation mechanism itself, which existed prior to the hormonal administration. This belief is supported, in part, by our observations on the patients with Addison's disease, with hypopituitarism, and on the individual with fatigue and diarrhea. All these persons had the expected high eosinophil counts of adrenal insufficiency and in all, the clotting times and protamine titers were above our upper limit of normal (0.10-0.14 mg for the latter). Abnormally high plasma-diluted

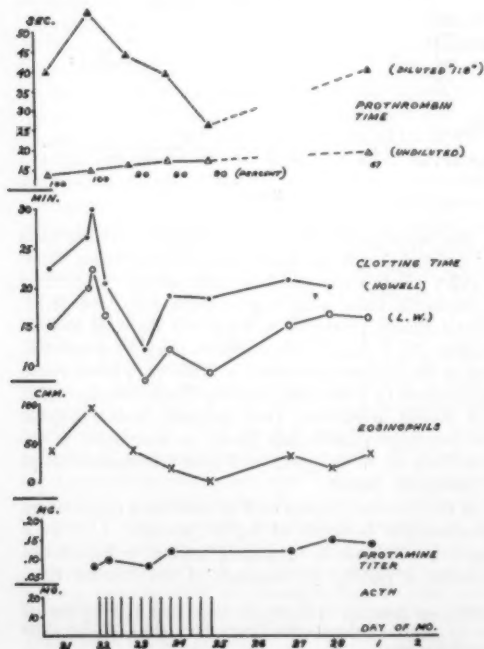


FIG. 2.

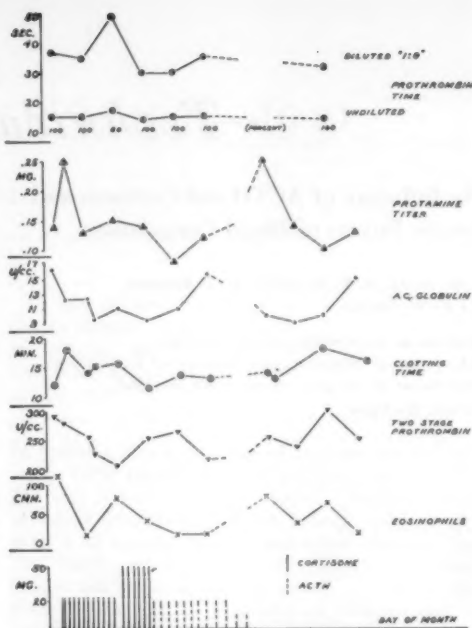


FIG. 3.

prothrombin times were observed in one Addisonian, whereas in 2 others the values were normal.

Fig. 2 demonstrates the profound changes in coagulation time that may follow ACTH administration. The clotting time by the two methods, in less than 24 hr, was reduced by 15 min. In this patient the reduction was paralleled by significant changes in the prothrombin system, as reflected in the marked shortening of the plasma-diluted prothrombin times. It is notable that the control level of circulating heparin or heparinlike material was so low as to suggest, and only suggest, a possible compensatory reduction for the initial prothrombin defect. In this individual, no significant increase in circulating heparin was observed at any time. The initial delayed diluted prothrombin time was not uncommonly encountered in this series. Of 20 patients adequately studied, 6 had the initial defect, and in every instance the diluted prothrombin time was brought to normal while ACTH or cortisone was being given.

In Fig. 4 are illustrated the changes that might be considered the most representatives of the series and that, in some respects, are similar to the alterations induced in the one normal male (Fig. 1) under continued ACTH administration. The following can be noted to have occurred: initial transient increase in protamine titers and clotting times; slight but significant lowering of clotting times during therapy and return to control level when the hormone was withdrawn; a varying increase in the level of circulating heparin or heparinlike material on therapy which, inexplicably, continued after ACTH withdrawal; significant changes both in the percent prothrombin and

the diluted prothrombin times, which appear inverse to the changes in protamine titers. These return to normal on completion of therapy and can be correlated with the level of adrenal cortical activity by the number of circulating eosinophils (plotted in the lower portion of the figure). Of 20 patients studied, following the first 24 hr of treatment, 12 had an over-all decrease, 6 had no significant change, one had an increase in clotting time, and one had insufficient observations to interpret adequately. Seven of 17 patients with normal initial values had a significant increase in the diluted prothrombin time on therapy. Two had lowered and 5 had elevated protamine

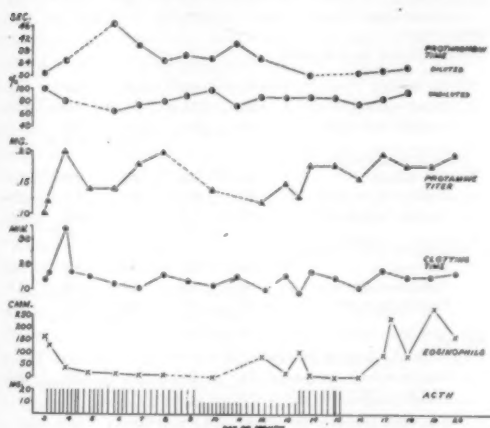


FIG. 4.

titers, of 17 patients in whom this was adequately studied during the period of hormone administration. In addition, there were several patients with high initial protamine titers and low initial eosinophil counts suggesting pre-existing stress, and in these significant changes on treatment were not observed. Platelet counts were not significantly altered.

Figs. 1 and 3 are presented to illustrate the influence of ACTH and cortisone on a number of humoral factors not covered above and known to be active in the coagulation process. It is apparent that variations were produced in the levels of plasma α -globulin and two-stage prothrombin (Fig. 3) and in α -globulin and antifibrinolytic (Fig. 1). At present the significance of these changes to blood coagulation in patients receiving ACTH or cortisone is not apparent and will not be further discussed. Similar observations have been made on 6 additional patients under hormonal treatment.

The results of the study herein reported do not allow any broad conclusions, inasmuch as the changes following ACTH and cortisone are by no means uniform from patient to patient. There is little question, however, that the adrenal cortex exerts an effect on a number of constituents of the clotting mechanism and, in some instances, may alter significantly the clotting time when its function is accelerated. The release of heparin or a heparinlike substance into the blood following ACTH or

cortisone may be akin to the hyperheparinemia of anaphylactic shock. It affords an additional link in our present understanding of the interrelationship of the mast cell with its heparin production, the adrenal cortex, and the changes in blood coagulability which may accompany the response to stress. The application of the results of the present study to the patient with adrenal insufficiency and to the patient undergoing surgery, among many problems, is obviously indicated and is being currently pursued.

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The Nucleus-Dependence of P^{32} Uptake by the Cell

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The various lines of evidence concerning the role of the nucleus in living cells converge in the hypothesis of an ill-defined "determination," or "control," function. The most complete evidence, that from studies of reproduction, heredity, and morphogenesis, is based on experimental designs that give little insight into the problem of the function of the nucleus in the current activities of the mature cell. The fragmentary information on this latter problem, derived from observations on cells deprived of nuclei, has generally been interpreted in terms of two hypotheses (1): (1) that the nucleus is a center of essential energetic processes and is immediately involved in the short-term metabolism of the cell, or (2) that the nucleus is concerned only with the long-term maintenance of the cytoplasm. The latter hypothesis derives from observations on cells whose nuclei have been removed. These may survive for some time (a few days to several months [4]) in terms of most identifiable activities, but ultimately they decline and die.

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² Atomic Energy Commission Postdoctoral Fellow, 1949-50.

For a closer analysis of this problem it is necessary, first, to identify those classes of reactions which are nucleus-dependent and, second, to watch their fate in time following removal of the nucleus. The present experiments deal with the nucleus-dependence of P^{32} uptake in *Amoeba proteus*. This large cell is favorable for removal of the nucleus or for other dissections. It survives for 7-14 days after separation of the nucleus, and the superficial behavior of the enucleated cell has been described thoroughly (3). Some data are available on the respiratory rate before and after enucleation (3). As will be shown, it is possible to measure the P^{32} uptake of only 30-50 cells.

All the cells used in the experiments were descendants of the same single cell. Large numbers of amoebae were first washed completely free of food organisms in phosphate-buffered inorganic culture medium (2), the electrolyte composition of which was the same as that of the medium used for stock cultures. Cells were cut, free-hand, into approximately equal halves by glass needles, and the nucleate and enucleate halves separated. Fifty to 100 half-amoebae of each class were then transferred into dishes containing 50 ml of medium, to which P^{32} had been added. A similar culture containing the same number of whole amoebae was set up. The radioactive medium contained about 10 microcuries of $P^{32}O_4$ per ml. The three cultures were kept at 20° C for 24 hr. The amoebae were then washed free from external P^{32} by successive transfers through nonradioactive medium, until samples of the medium showed no measurable traces of radioactivity. Counted numbers of cells were placed in small watch glasses and dried. Their radioactivity was determined by means of a thin-window G-M counter, shielded with 2 in. of lead. Repeated measurements, which included shifting of the sample-dishes and the taking of large numbers of counts, gave reproducible results, and the differences observed cannot be attributed either to statistical fluctuation, although some of the counts were only about 50-100% above background, or to geometry.

The experimental design minimizes certain sources of misinterpretation. The P^{32} uptake was measured in the absence of food organisms and was, therefore, uncomplicated by differences in feeding behavior. In fact, none of the cells divided under these conditions, and the nucleate fragments did not show regenerative growth. Thus, the experiments measure chiefly basal processes involving P^{32} uptake. The comparison of nucleate and enucleate halves was undertaken in order to equalize effects of the cutting operation itself. Moreover, the comparison of nucleate halves with whole amoebae could give a measure of the extent to which the P^{32} uptake was localized in the nucleus itself.

Since the cells were under microscopic observation throughout the series of transfers, there is no question of the viability of the enucleate half-amoebae 24 hr after enucleation, in so far as the term can be applied to a cell without a nucleus. The enucleate fragments tested afterwards showed the behavior pattern characteristic of such individuals, which, in the experience of the authors,

survive for 5-10 days before the onset of obvious cytolytic changes.

In considering Table 1, where each column represents

TABLE 1

	Test No.				
	1	2a	2b	2c	5
External P (mg/ml)	.037	.10	.10	.10	.10
External P^{32} (counts/min/ml)	2,560	7,168	6,016	2,560	2,690
Background (counts/min)	17	17	22	21	19
P^{32} Uptake (corrected for background)					
Intact amoebae					
No. tested	41	50	37	60	75
Total counts/min	59	120	81	50	135
Counts/min/cell	1.2	2.4	2.2	.73	1.8
			(2.6)*	(2.0)*	
Nucleate half-amoebae					
No. tested	53	45	34	75	57
Total counts/min	32	81	34	14	55
Counts/min/cell	.65	1.8	1.0	.19	.98
			(1.2)*	(.53)*	
Enucleate half-amoebae					
No. tested	80	38	42	87	65
Total counts/min	8	14	13	5	19
Counts/min/cell	0.10	.45	.26	.062	.29
			(.31)*	(.17)*	
Ratios (P^{32} uptake/cell in 24 hr)					
Nucleate half-amoebae	.54	.75	.46	.26	.53
Intact amoebae					
Nucleate half-amoebae	6.5	4.0	3.8	3.1	3.4
Enucleate half-amoebae					

* Corrected for decay.

an independent experiment, only the experimental values in the same column should be compared. The specific activity of the isotope varied, as did the total P, in the individual experiments. The ratios of the values for the P^{32} uptake by the three classes of cells are comparable for the several experiments. It is seen that the P^{32} uptake by the enucleate fragments is consistently lower, by a factor of 3 or more, than that of the nucleate fragments. This is a real deficit, for the uptake by the nucleate fragments averages only one-half that by the whole amoebae, the ratio fluctuating rather widely on either side of 0.5. Therefore, the uptake by the nucleate individuals depends on the amount of cytoplasm, suggesting that the nucleus itself is not taking up a significant proportion of the P entering the cell. This is not surprising. It has been found (6) on other types of cells that the rate of P turnover in the nondividing nucleus is considerably lower than the rate in the cytoplasm. In amoeba, where the nucleus/cytoplasm ratio is low, the P turnover in the nucleus would have to be very high indeed to make a significant fraction of the turnover by the whole cell.

It is concluded, therefore, that the nucleus plays some decisive part in the P^{32} uptake by the cytoplasm. In the absence of a nucleus, the uptake by the cytoplasm in 24 hr falls to one-third the normal value or less. A simple

calculation demonstrates that what is being measured includes incorporation of the P^{32} into organic constituents of the cell. In experiment 2a, for instance, the P^{32} concentration of the medium is represented by 7×10^6 counts/min/ml. Taking a value of 50×10^{-4} mm³ as the volume of a whole amoeba, the concentration of P^{32} in the cell is represented by about 2×10^6 counts/min/ml. There is, therefore, more P^{32} in the cell, by a factor of 50-100 for the several experiments, than could be accounted for by complete equilibration with inorganic PO_4 . As has been pointed out by others, it is difficult even with data of this type to exclude the possibility that the organic P turnover is limited by the diffusion of inorganic PO_4 . However, it has been shown in the case of other cells that the total P uptake is very closely dependent on metabolic variables (7), and it has been argued that the initial step in the uptake of PO_4 by the cell is not diffusion across the surface but incorporation into organic compounds (6). The conclusion that the present experiments demonstrate a nucleus-dependence of actual P turnover by organic constituents of the cytoplasm is considered probable. Current experiments in which the relative incorporation of P^{32} into various fractions is being determined should provide a more decisive test, as well as closer identification to those processes involving P turnover that are nucleus-dependent.

Although the experiments indicate that metabolic mechanisms in the cytoplasm which can be measured by P^{32} uptake are nucleus-dependent, and that the nucleus itself does not turn over a significant proportion of the P, the question of the nature of the nucleus-dependence remains unanswered. The total P^{32} uptake in 24 hr has been measured. Does the nucleus itself participate directly in the process in some way that does not involve its handling the P, or are we dealing with an indirect, long-term function of the nucleus (8)? Examples of the latter would be mechanisms whereby the nucleus was responsible for maintaining the submicroscopic structure of the cytoplasmic systems, or mechanisms whereby the nucleus was essential for the replacement of enzymes that "wore out" during the experimental period. The question may be answered by experiments in which the P^{32} uptake is measured during various intervals after enucleation. If the nucleus participates directly, the effect of enucleation should appear shortly after enucleation. If we are dealing with a replacement mechanism, the effect of enucleation should be more pronounced with time.

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The Use of a Radioactive Isotope in Determining the Retention and Initial Distribution of Airborne Bacteria in the Mouse¹

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In studies of experimental airborne infections, it is important to know the retained dose and the initial distribution of the inhaled material in the host. The classical technique of grinding tissues to determine their bacterial content (1) may be an unreliable measure of the viable organisms present. More recently, bacteria that have been radioactively "tagged" have been used in distribution studies following injection (2), as have aerosols of inorganic radioactive material following inhalation (7). We have employed aerosols of radioactively "tagged" organisms in determining the retention and initial distribution of *Pasteurella pestis* in mice.

A 24-hr culture of an avirulent strain of *P. pestis* was grown in heart infusion broth (Difco) at room temperature on a shaker operating at a rate of 96 oscillations per minute with a stroke of 3 in. Five ml of this culture was transferred to a 100-ml flask of fresh medium containing approximately 1 millicurie of radioactive phosphorus (P^{32}) as soluble phosphate, and incubated as before. The viable count of such a culture was 1.5×10^9 cells per ml. The organisms were collected by centrifugation (2,000 rpm), washed twice in heart infusion broth, and resuspended in the same medium to yield a concentration of about 1×10^{10} viable cells per ml. In this suspension, one radioactive count per second represented approximately 1×10^6 viable organisms. Additional washings reduced the radioactivity of the cells by uniform amounts (approximately 10%), presumably in consequence of leaching. Two washings were considered sufficient for this investigation.

Mice of the Namru strain (3) were exposed to aerosols produced by atomizing suspensions of "tagged" bacteria in the apparatus described by Leif and Krueger (6). The average particle diameter in the aerosol was approximately 1μ , as determined with the particle size analyzer described by Goldberg (4).

In the first series of experiments, groups of mice 6-8 weeks old, of both sexes, were exposed to the bacterial aerosol for 20 min. Samples of the aerosol were collected by capillary impingers during the exposure to determine the concentration of radioactive material. Exposed animals were sacrificed within 30 min, skinned, and bled just below the diaphragm. The thoracic portions

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² The opinions and assertions contained in this report are the private ones of the writers and are not to be construed as official or reflecting the views of the Navy Department or of the naval service at large.

of the mice were heated individually in a muffle furnace at 300° F for 24 hr. The temperature was then raised to 1,000° F for 2 hr, and the radioactivity of the ashed remains determined. Another series of animals was similarly exposed but ashed *in toto* so that total retention in the animal could be ascertained.

Computation of the respiratory volume of the mice as a function of body weight was based on Guyton's (5) data. The theoretical dose received by each mouse was calculated from the computed respiratory volume and the concentration of the aerosol according to the following formula:

$$\text{Dose in cts/sec} = \frac{(\text{Wt of mouse, g}) (1.25) (\text{Exposure time})}{(\text{Cloud concentration})} \times 1,000$$

The results obtained in these experiments, presented in Table 1, indicate that the average respiratory retention

TABLE 1

PERCENTAGE RETENTION OF RADIOACTIVE MATERIAL IN MICE EXPOSED FOR 20 MIN TO AN AEROSOL OF *P. pestis* "TAGGED" WITH RADIOACTIVE PHOSPHORUS (P^{32})

No. mice	Calculated dose in counts/sec/mouse	Retention in respiratory tree		Retention in entire body	
		Counts/sec	% retention*	Counts/sec	% retention*
72	6.8	1.9	28
72	58.0	12.9	22
72	20.1	6.7	33
96	12.5	3.4	27
24	14.0	13.7	98
24	33.4	25.6	77
24	15.3	13.0	82

$$* \% \text{ retention} = \frac{\text{cts/sec}}{\text{calculated dose in cts/sec}} \times 100.$$

of organisms inhaled under the conditions described was approximately 30% of the calculated dose per mouse. This value may be compared with the total retention, which appears to be over 80% of the calculated dose.

In subsequent experiments, groups of mice were exposed, sacrificed, and dissected to determine the initial distribution of the inhaled radioactive material. In these

TABLE 2

RETENTION AND DISTRIBUTION OF RADIOACTIVE MATERIAL IN MICE EXPOSED FOR 20 MIN TO AN AEROSOL OF *P. pestis* "TAGGED" WITH RADIOACTIVE PHOSPHORUS (P^{32})

No. mice	Distribution of inhaled material (percentage of total retained)						Percentage total retention
	Head	Lung and trachea	Remaining upper half	Stomach	Intestinal tract	Remaining lower half	
16	6	21	5	38	..	28	106
14	10	16	8	24	..	44	124
30	..	13	12	22	39	14	...
30	..	14	9	38	27	12	...

animals, the activity was individually determined in the head, lungs, and trachea, stomach, intestines, and the remaining thoracic and pelvic portions of the body.

From the results obtained (Table 2), it appears that approximately 30% of the retained material is to be found predominantly in the respiratory tree, as compared with about 70% predominantly in the gastrointestinal tract. The total body retention, determined on the first two groups of animals, was nominally equal to the theoretically inhaled dose.

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The Intracellular Distribution in Rabbit Liver of Injected Antigens Labeled with P^{32}

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The gross distribution of labeled antigens following their injection into animals has been studied by numerous workers. Azoproteins containing arsenic (4), iodoproteins labeled with I^{127} (5) or I^{131} (13), and intensely colored antigens obtained by coupling proteins with dyes (10, 11) have been found to be deposited chiefly in the organs of the reticuloendothelial system, particularly in the liver and in the bone marrow; these organs, as well as the lymphatic tissues (3, 14), are regarded as the most probable sites of antibody formation. By means of the fixation reaction between fluorescent antibody and deposited antigen, it was shown that the antigen undergoes a granular deposition in the cytoplasm (2).

In this paper we wish to report on the intracellular distribution of radioiodinated antigens in the morphological fractions of rabbit liver prepared by differential centrifugation. Rabbits were injected intravenously with 80-100 mg of radioiodinated ovalbumin or beef serum globulin containing about 10% iodine. The iodoproteins were prepared from crystalline ovalbumin (9) or beef serum pseudoglobulin (6) according to the procedure of Wormal (15); the KI_3 solution used had been permitted to equilibrate with carrier-free radioactive iodide. At various intervals of time (from 75 min to 48 hr) follow-

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² Public Health Service Predoctorate Research Fellow, National Institutes of Health.

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TABLE 1
ANALYSIS OF LIVER HOMOGENATE FRACTIONS OF RABBITS INJECTED WITH I¹²⁵-OVALBUMIN

Rabbit No.	30			31		
Injected antigen weight:	87 mg			80 mg		
activity (cpm):	1,374,000			819,000		
Time killed after injection:	9 hr			75 min		
Whole liver:						
	Wet weight (g)	Dry protein (g)	Activity of dry protein (cpm/g)	Wet weight (g)	Dry protein (g)	Activity of dry protein (cpm/g)
	60.0	13.5	1,230	64.5	13.0	8,800
Fractions:						
	Dry protein (g)	Activity of dry protein (cpm/g)	(%)*	Dry protein (g)	Activity of dry protein (cpm/g)	(%)*
Nuclear fraction	2.20	1,470	19.5	2.22	6,870	13.4
Mitochondrial fraction	2.00	3,430	41.5	1.89	31,400	52.2
Submicroscopic particulate fraction	2.80	625	8.7	1.96	8,980	15.4
Final supernatant	6.27	611	23.1	6.04	2,630	13.9
Total	12.77		92.8	12.11		94.9

* Percentage of the activity of the whole liver homogenate.

ing the injection, the animals (which had been fasted for 10-18 hr) were killed by exsanguination; their livers were removed, passed through a Latapie mill, and the pulp so obtained was homogenized to 10% in 0.88 M sucrose (S), using a glass homogenizer.

A portion of the homogenate (40 ml) was centrifuged three times at 600 *g* to obtain the nuclear fraction (N); centrifugation of the supernatant solution twice for 25 min at 20,000 *g* furnished the mitochondrial fraction (M). The submicroscopic particulate fraction (P) was obtained by diluting the supernatant solution to 0.25 M sucrose and centrifuging twice for 1 hr at 18,000 *g* (12). The first sediments of M and P were washed by resuspension and recentrifugation before being combined with the second sediments. The volumes of N, M, and P were brought to 25 ml, and the volume of the final supernatant (S) was between 200 and 215 ml. The entire fractionation procedure was performed at 0-5° C and required 6-7 hr.

In order to remove split products of the antigen, we added 4.25 ml of 40% trichloroacetic acid to 20-ml aliquots of the original homogenate and of fractions N, M, and P, and 21.2 ml to a 100-ml aliquot of fraction S. Using 10-ml portions of the solvents, the protein precipitates were then washed by centrifugation and resuspension three times with 7% trichloroacetic acid, twice with acetone, three times with ethanol, and again twice with acetone. The residues were dried at 55° C, weighed, pulverized, and spread evenly on aluminum planchets for counting by an end-mica-window Geiger tube. The sample thickness was consistent for the samples within each experiment and never exceeded 10 mg/cm², where only 5% of the activity was self-absorbed.

The activity of the iodoproteins injected into 7 rabbits varied from 700,000 to 3,000,000 cpm. The results of two typical experiments are presented in Table 1. The

mitochondrial fraction had not only the highest activity per g of dry protein of any fraction, but it also accounted for a larger portion of the total activity than any of the other 3 fractions of the liver homogenate. In all our analyses, we found that 31.9%-69.8% of the total activity of the liver was located in the mitochondrial fraction. The activity of the nuclear fraction, although lower than that of the mitochondrial, was considerable. That this activity was not due to contamination with mitochondria was shown by the fact that the activity of the nuclear fraction of a rabbit injected with iodobovine serum globulin increased from 8,530 cpm/g to 9,280 cpm/g when the fraction was rehomogenized with 0.88 M sucrose solution and resedimented as described above.

In order to evaluate the extent of nonspecific adsorption of iodoprotein to the fractions, we added 0.04 ml of 3.46% iodobovine serum globulin to 100 ml of a normal rabbit liver homogenate and fractionated the mixture in the usual manner. We found 7% of the added activity in the nuclear, 3% in the mitochondrial, and 83% in the supernatant fraction containing the submicroscopic particles.

An analysis of the activity of various organs of rabbit No. 30 gave the following results: liver 1,860, spleen 1,250, bone marrow 2,800, lung 171 cpm/wet g, and urine 6,000 cpm/ml. No activity was precipitated from the urine by trichloroacetic acid, showing that its high activity was due to split products of the antigen. When whole liver homogenates of this same animal were precipitated by trichloroacetic acid 1, 3, and 7.5 hr after homogenization, the activities of the protein precipitates were 1,860, 1,890, and 1,810 cpm/wet g, indicating that no appreciable autolysis had taken place in the chilled homogenate.

The fact that the bulk of the deposited antigen is found in the mitochondria indicates that these particles

are involved in the formation of antibodies. As has been emphasized elsewhere (7), antibody formation can be interpreted as protein synthesis modified by the presence of antigen molecules. Actually, mitochondria have been considered to be endowed with the property of self-duplication (1), which implies protein synthesis.

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The Differential Induction of Lethal Mutations by Formalin in the Two Sexes of *Drosophila*¹

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Several studies have been made recently in an attempt to administer chemical mutagens to eggs and sperms at various stages in ontogeny, followed by tests to detect variation in the mutation rate. It was shown that, whereas sex-linked recessive lethal mutations were induced in both eggs and mature sperms of adult *D. melanogaster* after vaginal douches with the N mustard methyl bis (β-chloroethyl)amine hydrochloride (6, 7), there was no increase in the number of such mutations in either type of gamete when larvae were exposed to sublethal concentrations of this substance in the food (8). On the other hand, vaginal douches with formaldehyde failed to increase the mutation rate in eggs and mature sperms (7) but, although female larvae were not studied, large numbers of lethals occurred in the sperms of male larvae grown on food containing this chemical (8, 9, 11). Auerbach (8) has reported that formaldehyde fails to induce mutations in either type of gamete,

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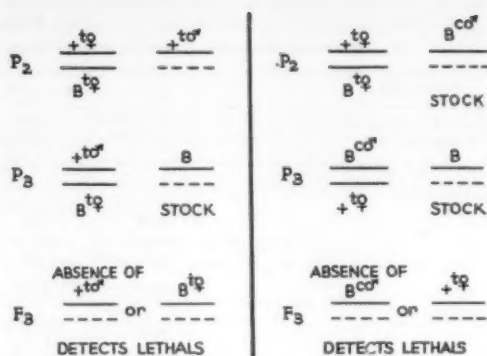


FIG. 1. Plan of matings to detect X-chromosome recessive lethals in progeny from P₁ crosses of Ore-R ♀♀ (+/+) by M-5 ♂♂ (B/Y). All ♀♀ virgin; all matings but P₁ in single pairs; solid line = X, broken line = Y chromosome; t = treated, c = untreated chromosome; ♀ or ♂ = P₂ parent from which chromosome came; up to 10 P₂ matings from each P₁ cross.

mature or immature, when this substance is administered directly. She has presented evidence suggesting that an active mutagenic agent is produced only when formaldehyde is first mixed with the food. The ability of a chemical substance to induce mutations with some techniques and not with others may have several possible explanations (1, 4, 7). Such factors as the solvent for, the concentration of, and the duration of treatment with the chemical substance used may account for the results obtained with different techniques.

In the experiments reported here, *D. melanogaster* Oregon-R wild-type ♀♀ were crossed to Muller-5 ♂♂ and permitted to oviposit for 2 days in bottles containing 50 ml of a standard culture medium. After removal of the parents, 0.75 ml of a 8.9–17.8% solution of formaldehyde was added by pipette on top of the food, and the F₁ ♀♀ and ♂♂ were permitted to complete their development. For the P₂, half the F₁ ♀♀ were crossed to F₁ ♂♂, the other half to stock (untreated) Muller-5 ♂♂. The detailed plan of matings to detect sex-linked recessive lethal mutations arising in the gonads of P₂ parents is presented in Fig. 1. These lethals, detected in the F₃ generation, are of the following 4 types: + chromosome from treated F₁ ♀♀ (+t♀); B chromosome from treated F₁ ♀♀ (Bt♀); + chromosome from treated F₁ ♂♂ (+t♂); B chromosome from untreated P₂ Muller-5 ♂♂ (Bcd♂). Lethals were retested for confirmation (7). The results are presented in Table 1.

A total of only 10 lethals occurred in 4,493 X chromosomes tested from control males (Bcd♂) and treated

TABLE 1
TYPE OF LETHAL

	+t♀	Bt♀	+t♂	Bcd♂
No. lethals	3	4	57	3
No. X chromosomes tested	1,546	1,401	1,401	1,546

female larvae (+ φ and B φ). However, in the 1,401 X chromosomes tested from treated male larvae (+ σ), there were 57 lethals arising from 47 independent origins. Although this increase in the mutation rate of treated males is comparable with the results obtained by others (8, 9, 11), the mutation rate of females treated in the same environment is not detectably different from that of the untreated controls. Differential frequencies of lethals in the two sexes have been reported previously for spontaneous mutation (8) and for mutations induced by mustard gas (8), x-rays (5), and P³² (10). Whether this sexual difference in mutation rate is due to some morphological or physiological difference between male and female *Drosophila* or whether it is due to an innate difference in the mutability of the sex cells themselves remains undetermined. Nevertheless, should this type of phenomenon prove to be of general occurrence it would have interesting implications concerning the function of sex in the statics and dynamics of evolution.

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Lethal Mutation Rate in *Drosophila* Treated with 20-Methylcholanthrene¹

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Reports on chemical mutagenesis (8) have revived the old idea that mutations are responsible for cancer. A number of authors have inferred that the parallelism between mutagenic and carcinogenic properties of certain chemicals lends support to this hypothesis (6, 14). The data presented are results of tests for the possible mutagenic activity of the carcinogen 20-methylcholanthrene in *Drosophila melanogaster*.

In the first group of experiments, virgin, heterozygous females derived from the Oregon-R and Muller-5 stocks were treated with 1% 20-methylcholanthrene in sesame oil by the vaginal douche technique described by Herskowitz (8). The carcinogen used was from a solution which previously had been tested and found to be fully potent in producing sarcomas in C₃H and JK mice and their progeny (4). It was injected into the vagina, which was

partially everted by lateral pressure on the abdominal wall. Adult females 3 days old were treated and mated individually to Muller-5 males 5 days old. The male was removed after 24 hr and the female allowed to oviposit for 3 days in each of 3 vials. One portion of the offspring was then tested for lethals and another group treated, repeating this each generation.

The Muller-5 method of testing for recessive lethal mutations on the X-chromosome was utilized. Ordinarily the Oregon-R/Muller-5 heterozygous female has both wild type (+) and *sc^a w^a B* sons. However, if a lethal is present on the chromosome from the Oregon-R stock, only *sc^a w^a B* males appear among the offspring. Conversely, a lethal present on the Muller-5 (*sc^a w^a B*) chromosome will result in + offspring only. The advantages of the method in this investigation are that heterozygous females which appear each generation may be used subsequently for retesting for lethals when poor cultures are obtained, and serial treatment is possible. In all cases where lethals were suspected, the chromosome was retested by the same method. All lethals reported have shown no male bearing the lethal chromosome among at least 50 males of the opposite type. Every lethal was retested at least once. The vaginal douche treatment was continued serially for 11 generations over a period of 128 days, mating females heterozygous for the wild-type and Muller-5 chromosomes to Muller-5 males. Since the wild-type chromosome may be recovered in the female progeny in each generation, it is possible to continue treatment of the chromosome in subsequent generations. The wild type chromosome tested in each successive generation had therefore been treated from 1 to 11 times. The total period of treatment of the + chromosome, therefore, was longer than the time required to induce tumors with this carcinogen in certain strains of mice (5).

The investigation originally was designed to test the effect of serial administration of the carcinogen on mutation rate, but, when it was found that very few mutations appeared, a different method for administering the chemical was adopted. In the second series of experiments Oregon-R males were treated with 1% 20-methylcholanthrene in sesame oil in the form of an aerosol with air flowing through the nebulizer at the rate of 6 l per min for a period of 30 sec every 30 min. The lethal mutation rate was then determined by the Muller-5 method for flies treated 15, 24, 48, 72, 96, and 216 hours, respectively.

Control values for mutation rate were obtained by mating females heterozygous for the Oregon-R and Muller-5 chromosomes to Muller-5 males, rather than obtaining the rate in each stock separately. The medium used contained Cream of Wheat, molasses, agar, and yeast. The matings were made in vials and the temperature was maintained at 25° C.²

There was a high mortality with both forms of treatment. It was found that 52% of the females died following vaginal douche and that only 37.2% of those surviving were fertile. Most of those that were sterile laid

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² The author is indebted to Betty Rosenbohm for her excellent technical assistance.

TABLE 1
LETHAL MUTATION RATE AFTER SERIAL ADMINISTRATION OF 20-METHYLCHOLANTHRENE IN A VAGINAL DOUCHE

Gener- ation	Females injected	Females tested	Chromo- somes tested	Lethal mutations						Visible		Nondis- junction	
				+ chromosome		B chromosome		Total		Total			
				No.	%	No.	%	No.	%	No.	%	No.	%
1	36	2	86										
2	54	3	54										
3	56	35	1,224			1	.163	1	.082	1	.163	1	.163
4	39	28	1,116										
5	27	18	676										
6	34	10	224										
7	50	19	398			1	.503	1	.251				
8	34	9	206										
9	35	2	22										
10	30	16	500										
11	34	7	154	1	1.299	1	0.649
Total	429	149	4,660	1	.043	2	.086	3	.064	1	.021	1	.021

no eggs (59.2% of the total), doubtless as a result of the trauma. (The number of males dying after administration of aerosol appears in Table 2.)

The lethal mutation rate following serial administration of 20-methylcholanthrene in a vaginal douche was found to be .064%. The rates for each generation in the series appear in Table 1. One mutation on the + chromosome appeared in the 11th generation, and one occurred on the *sc*⁸ *wa* B chromosome in the 3rd and one in the 6th generation. These three lethal mutations occurred among 4,660 chromosomes tested. In the 4th generation a *yellow* male was found when tests were made for lethals. This gene was present on the wild-type chromosome. An instance of nondisjunction of the X-chromosome was found and confirmed in subsequent generations.

When the carcinogen was administered as an aerosol (Table 2), 5 lethal mutations were found on the + chromosome and 5 on the *sc*⁸ *wa* B chromosome among 10,108 chromosomes tested, a mutation rate of .099%. It should be noted that only the + chromosome was treated by this method. Lethals occurred in the groups treated 15, 72, and 216 hours, but not in those when the treatment period was 24, 48, and 96 hours. Two of the lethals on the + chromosome occurred among 12 offspring of a single male. Also in the progeny from each of two other matings there were two lethals on the

*sc*⁸ *wa* B chromosome. More offspring had been tested, however, 85 in one instance and 26 in the other.

Demerec (6, 7) has reported a number of carcinogenic compounds to be mutagenic and has included 20-methylcholanthrene among them. Sacharow (13) obtained 18 lethals in 2,921 chromosomes by treating *Drosophila* eggs with methylcholanthrene, and 87 lethals among 33,975 chromosomes tested in the control series.

Preliminary experiments with feeding carcinogens gave negative results in experiments by Auerbach, and, later more extensive studies on mutation rate following the injection of carcinogens, including methylcholanthrene, also gave negative results (1). Bhattacharya (3) found no increase in mutation rate when methylcholanthrene was fed to larvae. It is pointed out in the report that there is no significant difference between the positive results reported by Demerec and the results Bhattacharya obtained in the feeding experiments, although the latter were negative when compared to controls.

The use of mice in quantitative work on mutations has definite limitations and is the reason this investigation was done with *Drosophila*. The detection of visible mutations is somewhat subjective, and inversions are not available for use in detecting lethal or visible, recessive mutants. There is the undeniable advantage, however, that mice bear tumors very similar to those in man.

TABLE 2
LETHAL MUTATION RATE (20-METHYLCHOLANTHRENE AEROSOL)

Treat- ment period	Died with treatment	Males tested	Chromo- somes tested	Lethals					
				+ chromosome		<i>sc</i> ⁸ <i>wa</i> B chromosome		Total	
				No.	%	No.	%	No.	%
15 hr	26	51	1,484	1	.135			1	.067
24 hr	1	41	1,858						
48 hr	10	51	1,060						
72 hr		41	1,786	3	.336			3	.168
96 hr	21	19	290						
216 hr	71	74	3,630	1	.055	5	.275	6	.165
Total	129	277	10,108	5	.099	5	.099	10	.099

TABLE 3
LETHAL MUTATION RATE

Treatment	Chromo- somes tested	Lethals						P
		+ chromosome		sc ⁸ w ⁸ B chromosome		Total		
		No.	%	No.	%	No.	%	
Control	2,822	1	.071	1	.071	2	.071	
20-Methylcholanthrene (vaginal douche)	4,660	1	.043	2	.086	3	.064	0.09
20-Methylcholanthrene (aerosol)	10,108	5	.099	5	.099	10	.099	0.7

Strong (14) has reported numerous variants in strains treated with 20-methylcholanthrene for a number of generations, including color changes and differences in susceptibility to tumors. He regards these as mutations induced by the chemical and thinks it is probable that methylcholanthrene may bring about malignancy by causing somatic mutations. In commenting on this work, Auerbach (8) has questioned the accuracy of the comparison of the experimental mutation rate (1 in 557) to the control (1 in 26,250) given by Strong, although she was impressed by the large number of variants in an animal in which visible mutations rarely occur.

Tatum (15) has reported the appearance of 6 biochemical mutant strains among 2,075 cultures of *Neurospora* treated with 20-methylcholanthrene endosuccinic acid. One apparently contained 2 independent gene mutations. Control studies from another of his experiments showed 1 biochemical and 6 morphological mutants. He mentioned a high incidence of morphological mutants with methylcholanthrene but did not feel that a significant difference had been established by the data at hand. He did, however, state that results with *Neurospora* suggest that this carcinogen has mutational effects. On the other hand, Latarjet (11) found no increase in mutation rate when methylcholanthrene was used to treat bacteria, even though enough of the chemical was present to cause the organisms to fluoresce.

The figures for mutation rate in *Drosophila* obtained in these experiments reveal that there is no significant difference (Table 3) between control rate and that for treatment by vaginal douche ($P=0.99$) or for treatment with methylcholanthrene aerosol ($P=0.7$). The appearance of a yellow male and the instance of nondisjunction are not regarded as evidence to the contrary. The experiment was not designed for determining the rate of visible mutations or the incidence of nondisjunction. Also, yellow is known to mutate spontaneously more frequently than many other loci in *Drosophila*.

The discrepancy between these and other negative findings and those which have indicated that 20-methylcholanthrene is mutagenic may be explained in several ways. It is possible that the carcinogen was not present in optimum concentration over a sufficient period to be effective as a mutagen. It is also possible that the route of administration or the vehicle in which it was given did not allow access to the chromosomes. Finally, mutagenic effects may be strain- or species-limited.

Factors which would operate toward giving false negative results were minimized as much as possible. The

concentration of carcinogen used was sufficiently high so that further increase does not reduce the induction time of subcutaneous tumors in inbred mice, although the high concentration is not necessarily optimum. More than one route of administration of the carcinogen was utilized, and both methods have given positive results with nitrogen mustard in other work by the author. Chromosomes from the males were treated by means of the aerosol, and those from both males and females by the vaginal douche technique. In the latter the treatment was repeated and perhaps prolonged. The stock of Oregon-R used was obtained from the laboratory of Dr. Demerec, and the aerosol method he described (7) was duplicated as nearly as possible.

Undoubtedly chemicals can induce mutations. Some of these chemicals are also carcinogens. For example, methyl-bis(β chloroethyl)amine hydrochloride (2) and urethane (16) are capable of inducing mutations and also of increasing the incidence of mouse tumors (9, 13). Others, such as formaldehyde, are mutagenic (10) but not carcinogenic. There is little basis at the present time, however, for the assumption that all carcinogens are mutagens. Even in the reports of Demerec (6), there are negative results for agents known to be carcinogenic. The results reported in this communication do not support the hypothesis that 20-methylcholanthrene is a mutagen, since the mutation rate of lethals on the X-chromosome was not increased either by administering 1% 20-methylcholanthrene in sesame oil by vaginal douche serially for 11 generations over a period of 128 days or as an aerosol during periods of from 15 to 216 hours. More work is in order to clarify the reasons for the differences in results with this carcinogen. There would seem to be a reasonable doubt that there is necessarily a connection between mutagenic and carcinogenic effects of an agent or that carcinogens are necessarily mutagens. At the present time there are even more obstacles in accepting without reservation the hypothesis that tumors are the direct result of somatic mutations.

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Arylcycloalkylamines

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Sympathomimetic amines in which the basic side chain is part of a saturated ring not condensed with their aro-

1 mm) by the slow methanol catalyzed reaction of cyclohexanone and phenyldiazomethane in a yield of 43%. The ketone yielded 2-phenylcycloheptylamine by the Leuckart reaction, and 5,5-(2'-phenylhexamethylene) hydantoin by the Bucherer method. In a similar way, 2-methylcycloheptanone (8) furnished 2-methylcycloheptylamine, and 5,5-(2'-methylhexamethylene) hydantoin, respectively. 4-Methylcycloheptylamine was prepared from 4-methylcycloheptanone (5).

Structural analogues of Methadon were obtained by subjecting 2,2-diphenylcyclohexanone (4) to the Mannich reaction with secondary amines. The resulting 6-dialkylaminomethyl-2,2-diphenylcyclohexanone derivatives, and the corresponding amino alcohols, are listed in Table I. 2,2-Diphenyl-6-bromocyclohexanone, obtained from the parent ketone by bromination, has also been converted to 2,2-diphenyl-6-dialkylaminocyclohexanone derivatives.

TABLE I
PHYSICAL PROPERTIES AND ANALYSES OF SUBSTITUTED CYCLOALKANE DERIVATIVES

Compound	Mp, °C	Formula	Percentage composition	
			Calculated	Found
2-Phenylcycloheptanone semicarbazone	154-156	C ₁₄ H ₁₉ N ₃ O	N, 17.13	17.42
2-Phenylcycloheptylamine · HCl	196.5-197.5	C ₁₅ H ₂₀ ClN	C, 69.16 H, 8.93 N, 6.20	68.52 8.95 6.45
5,5-(2'-Phenylhexamethylene) hydantoin	204.5-207.5	C ₁₅ H ₁₈ N ₂ O ₂	C, 69.74 H, 7.02 N, 10.85	69.57 7.00 10.89
2-Methylcycloheptylamine · HCl	225.5-227.5 (dec.)	C ₈ H ₁₈ ClN	C, 58.70 H, 11.08 N, 8.56	58.63 10.91 8.45
5,5-(2'-Methylhexamethylene)hydantoin	216-218.5	C ₁₀ H ₁₈ N ₂ O ₂	C, 61.20 H, 8.22 N, 14.28	61.30 8.74 14.78
4-Methylcycloheptylamine · HCl	207-209	C ₈ H ₁₈ ClN	C, 58.70 H, 11.08 N, 8.56	59.24 11.21 8.27
2,2-Diphenyl-6-dimethylaminomethylcyclohexanone	106-107	C ₂₁ H ₂₇ NO	C, 82.04 H, 8.20	82.18 8.18
2,2-Diphenyl-6-dimethylaminomethylcyclohexanol	108.5-109.5	C ₂₁ H ₂₇ NO	C, 81.51 H, 8.80	81.35 8.80
2,2-Diphenyl-6-morpholinomethylcyclohexanone · HCl	160	C ₂₈ H ₂₉ ClNO ₂	C, 71.58 H, 7.31	71.78 7.54
2,2-Diphenyl-6-bromocyclohexanone	117-119.5	C ₁₈ H ₁₇ BrO	C, 65.06 H, 5.21	65.69 5.39
2,2-Diphenyl-6-morpholinocyclohexanone	124.5-125	C ₂₈ H ₂₉ NO ₂	C, 78.77 H, 7.51	78.98 7.71
2,2-Diphenyl-6-piperidinocyclohexanone	121.5-122	C ₂₈ H ₂₇ NO	C, 82.84 H, 8.16	83.12 7.63

matic portion have been the subject of recent studies (1). The excellent paper by Gutsche (3) concerning ring enlargements with diazomethane and phenyldiazomethane prompts us to record similar reactions used by us for the preparation of intermediates in the synthesis of phenyl- and diphenylcycloalkylamines in an extension of this series.

We prepared 2-phenylcycloheptanone (bp 133°-137°,

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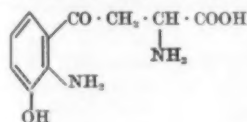
Crystalline + Chromogen Obtained from *Bombyx mori*

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Corresponding to the en⁺-substance of *Drosophila* and A-substance of *Ephestia*, +chromogen (W-substance of *Bombyx*) is widely distributed among insects and other arthropods. Most of its chemical nature, including its structure, has been obscure, except that one of us (3) in 1943 isolated a minute amount of a crystal-like substance which seemed to be +chromogen. Recently W. Weidel (1,2), of the Kaiser Wilhelm Institut für Biochemie, has isolated the en⁺-substance from larvae of *Calliphora erythrocephala* and stated it to be 3-hydroxykynurenine, which was postulated by Mitchell and Nye (4) to be a precursor of nicotinic acid, but the details are unknown.

The authors have isolated 50–60 mg of light-yellowish crystals from 400 g of new-laid eggs of *Bombyx mori*. The qualitative chemical nature of this crystalline substance, as well as results of biological tests, provides convincing evidence for considering it to be +chromogen. Elementary analysis and certain aspects of chemical behavior coincide with the structure shown in Fig. 1, but



(I)

FIG. 1.

direct proof is not yet available. The synthesis of 3-hydroxykynurenine, which is at present in progress, will determine the validity of this postulated structure. The isolation was carried out by modifying the method of Kikkawa (3).

Within 24 hr after oviposition 400 g of eggs of the normal type were killed in methanol, the methanol discarded, and the eggs carefully ground. This was extracted at 75° C with methanol until the extract and residue showed a negative Ehrlich's reaction. Methanol was thoroughly removed by concentrating the combined extracts *in vacuo*, and the remaining aqueous solution was washed with ether and the ether then removed. Hopkins-Cole's reagent was added, and the mixture was left in an icebox for 2 days, when precipitates appeared. These were suspended in 2% H₂SO₄; H₂S was passed through the suspension, and the resulting HgS discarded. The filtrate was concentrated to a H₂SO₄ concentration of 5% and 2–3 vol of 20% phosphotungstic acid in 5% H₂SO₄.

¹ The authors wish to acknowledge their indebtedness to F. Egami for his advice and encouragement during the course of this work, and to K. Yamasaki and K. Sone for the measurements of the ultraviolet spectra.

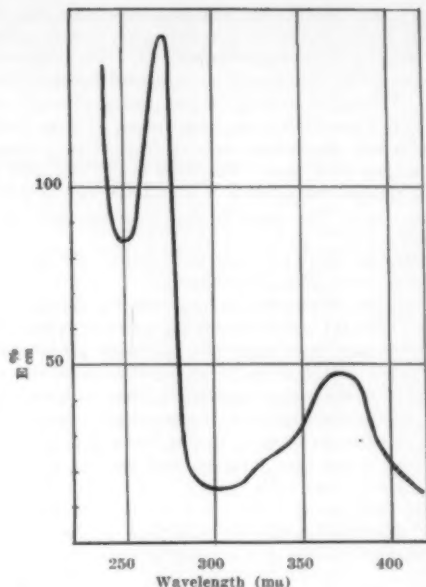


FIG. 2. Absorption spectrum of +chromogen in water.

Abs. maximum: 270 mμ (E_{1%}^{1cm} = 143).

370 mμ (E_{1%}^{1cm} = 46).

were added. The solution was ice-cooled one night, whereupon precipitates of +chromogen separated. After being washed with the phosphotungstic acid solution, the precipitate was added to 5% H₂SO₄, and the phosphotungstic acid solution removed by shaking with an ether-amyl alcohol mixture (125:100). A small amount of precipitate was filtered, and BaCO₃ added till the solution became red against Congo red. The BaSO₄ precipitate was washed thoroughly until the washing liquid was negative to Ehrlich's reagent. The filtrate was added to the original solution, and the combined solutions concentrated *in vacuo*, when a yellow-brownish solid was obtained. This was extracted several times with methanol; +chromogen dissolved, leaving an insoluble brownish mass. The extracts were concentrated *in vacuo* and left in an icebox; crystalline +chromogen separated. If necessary, the methanol-extraction was repeated. The crystals could be recrystallized from a small amount of water. Yield: 50–50 mg; 3–4 mg of the substance was also obtained from eggs of the white-2 mutant of *Bombyx mori*. The crystals, light-yellowish needles, mp 180° C (accompanying decomposition), possessed approximately 1 mole of water of crystallization, which was removed by heating to 100° C *in vacuo* for 2 hr.

Anal. calculated for structure I (C₁₀H₁₂O₄N₂):

C 53.59, H 5.40, N 12.49.

Found: C 52.23, H 6.04, N 12.80.

Assuming that the substance obtained is actually 3-hydroxykynurenine, the analytical data suggest that a further amount of water of crystallization may still re-

main. The ultraviolet absorption spectrum (Fig. 2) closely resembled that of kynurenine, but it gave a negative Otani's kynurenine reaction (5). The ninhydrine, xanthoprotein, and Ehrlich's diazo reactions were positive. The alkaline solution was of a deep-yellowish color and gave a jasminalike odor when heated. Dilute KMnO_4 solution also changed the color to deep yellow (urochromogen test of Weiss). The Folin-Denis' uric acid reagent changed the solution to a greenish, and then to a bluish, color. The murexide and lumiflavin tests were negative.

Biological tests employing the mutants vermilion and cinnamon of *Drosophila* were positive.

Addendum: In a previous paper in this journal (*Science*, 1950, 111, 608) concerning the tryptophan pigments, which dealt with the epidermis pigments of the yellow mutant "Jem" of *Bombyx mori*, we reported that the yellow pigment was xanthopterin, but, according to direct comparison with a sample of xanthopterin (kindly sent by E. L. Rickes, Merck & Co., Inc.) it has been found that, although this pigment resembles xanthopterin remarkably closely, it is slightly different. It has been named xanthopterin-B (B from *Bombyx*), and 2 other new pterins have also been isolated (leucopterin-B and a 6-dehydroxyleucopterin derivative) (6).

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Built-up Poultry-House Litter as a Growth-promoting Supplement for Chicks on an All-Vegetable Vitamin B_{12} -deficient Diet

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Extensive trials by Kennard and Chamberlin (1, 2) at the Ohio Agricultural Experiment Station demonstrated that poultry-house floor litter which has accumulated (built up) for a long period of time gives better chick growth on all-vegetable diets than litter which is completely changed at frequent intervals. Reports have also been made regarding improved hatchability of eggs from hens on such litter (3, 4). It has been found that poultry droppings contain the "animal protein factor" (APF) (?), and that incubation of hen feces for 72 hr at 30° C stimulates further synthesis of this factor (4).

In a series of studies dealing with the synthesis of vitamin B_{12} (now recognized as being an important part

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of the animal protein factor) by microorganisms in poultry-house litter, marked stimulation of growth was secured by adding built-up litter to an all-vegetable vitamin B_{12} -deficient diet fed to S. C. White Leghorn chicks in a wire-floored battery brooder.

The basal diet used was one consisting principally of soybean oil meal and ground yellow corn supplemented with the known requirements for vitamins, minerals, and the amino acid methionine. The diet was used for studies of soybean oil meal and animal protein factor by workers at the Purdue Agricultural Experiment Station (5, 6).

Vitamin B_{12} was shown to be the principal deficiency in the basal diet by the marked stimulation of growth secured by intramuscular injection of a saline solution of crystalline vitamin B_{12} (Cobione)² given in the amount of 0.3 μg per chick weekly. This injection was as effective in stimulating chick growth as feeding the crude APF supplement³ containing the equivalent of 20 μg of vitamin B_{12} /kg of diet.

As shown in Table 1, addition of 1%, 2.5%, and 5%

TABLE 1
EFFECT ON CHICK GROWTH OF ADDING BUILT-UP POULTRY-HOUSE LITTER AND OTHER SUPPLEMENTS TO AN ALL-VEGETABLE VITAMIN B_{12} -DEFICIENT DIET

Diet	No. Trials	Total No. chicks at start	No. died	Avg 6-wk wt in g (all trials)	Feed per g gain
Basal vitamin B_{12} -deficient diet	3	53	8	345	3.78
Basal + APF supplement*	3	53	4	429	3.23
Basal + vitamin B_{12} injections†	1	15	1	426	3.02
Basal + 2.5% ground corncoals	1	15	1	250	5.16
Basal + 5% ground corncoals	1	15	1	265	4.85
Basal + 1% unautoclaved built-up litter	1	18	0	419	3.04
Basal + 1% autoclaved built-up litter	1	18	1	394	3.28
Basal + 2.5% unautoclaved built-up litter	3	53	3	390	3.29
Basal + 2.5% autoclaved built-up litter	2	38	0	466	2.82
Basal + 5% unautoclaved built-up litter	2	27	3	412	3.34
Basal + 5% autoclaved built-up litter	2	35	0	493	2.55

* Twenty μg vitamin B_{12} /kg of diet.

† Crystalline vitamin B_{12} (0.3 μg /chick weekly).

levels of screened unautoclaved built-up corncoals litter (over 1 year old) to the basal diet gave increased chick growth to 6 weeks of 74, 45, and 67 g, respectively, as compared to 84 g for the added APF supplement fed at the rate of 20 μg of vitamin B_{12} /kg of diet. The built-up litter used for chick feeding was accumulated from hens that had been fed an all-vegetable vitamin

² We are indebted to Merck & Co., Inc., Rahway, N. J., through the courtesy of D. F. Green, for the crystalline vitamin B_{12} (Cobione) and the APF supplement (crude vitamin B_{12}) used in these studies.

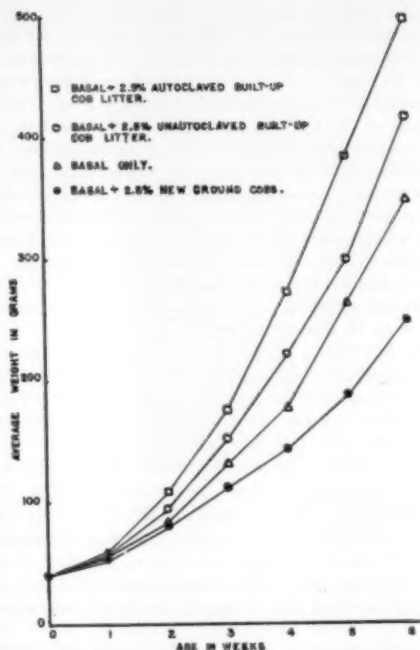


FIG. 1. Chick growth on all-vegetable vitamin B₁₂-deficient basal diet vs. basal plus 2.5% of various kinds of litter.

B₁₂-deficient diet. The autoclaving of this built-up litter for 15 min at 15 lb pressure made it decidedly more effective at the higher levels and produced a growth stimulation of 49, 121, and 142 g for the 1%, 2.5%, and 5% levels, respectively. Addition of ground corn-cobs to the basal diet, at the rate of 2.5% and 5%, decreased growth by 95 and 80 g, respectively (Fig. 1).

Autoclaving of the built-up litter may release a bound form of vitamin B₁₂, or it may destroy a toxic factor in unautoclaved litter that has a counteracting inhibitory effect on chick growth used at fairly high levels. The increase in growth obtained upon adding 1% of unautoclaved built-up litter as compared to 2.5% tends to support the theory that a toxic factor is present in the litter that has an inhibitory effect on growth, and that this factor is destroyed by autoclaving.

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Preliminary Results on the Crystal Structure of Some Ammonium Salts with Substituted Aliphatic Chains

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Because of renewed interest in the structure of aliphatic compounds, especially amines with straight and branched chains, preliminary investigations have been made upon the normal temperature modifications of the dodecyl-, tridecyl-, tetradecyl-, hexadecyl-, and α -methyl-dodecyl-ammonium chlorides. Dodecylammonium, tetradecylammonium, and hexadecylammonium chlorides are monoclinic, space group $P2_1$ or $P2_1/m$, with $n=2$. Chemical considerations give preference to $P2_1$. Tridecylammonium chloride is orthorhombic, space group $C2ca$ or $Cmca$, with $n=8$. Cell dimensions of these compounds are:

	a	b	c	β
$C_{12}H_{25}NH_4Cl$	5.66 Å	7.15 Å	17.73 Å	92° 30'
$C_{14}H_{29}NH_4Cl$	5.67 Å	7.20 Å	20.13 Å	95° 52'
$C_{16}H_{33}NH_4Cl$	5.71 Å	7.24 Å	22.56 Å	98° 21'
$C_{18}H_{37}NH_4Cl$	7.57 Å	7.61 Å	56.49 Å	90°

N-methyl-dodecylammonium chloride is triclinic, space group $P1$, with $n=2$. Cell dimensions are: $a=4.98$ Å; $b=5.29$ Å; $c=29.92$ Å; $\alpha=90^\circ 52'$; $\beta=91^\circ 52'$; $\gamma=90^\circ 45'$.

The Buerger precession camera was used almost exclusively for unit cell and space group determinations. Laue photographs of these compounds, especially dodecylammonium chloride, show strong diffuse reflections which will be further investigated.

Patterson-Harker projections have been completed, and Fourier analyses are under way on molecular configurations and bond lengths.

¹This work is being carried on under a fellowship sponsored by Armour and Company.

Growth Layers on the Teeth of Pinnipedia as an Indication of Age

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Government biologists engaged in research on the Alaskan fur seal, *Callorhinus ursinus* (L.), in recent years have marked 80,000 young seals by means of hot-iron brands or numbered metal tags. As a result, thousands of animals of known age are now available for study on the Pribilof Islands, in the Bering Sea, where the adult seals gather each summer to breed, and the young seals to rest. While examining the skull of a known-age specimen in 1949 we observed faint concentric ridges around the roots of the teeth. The age of the seal in

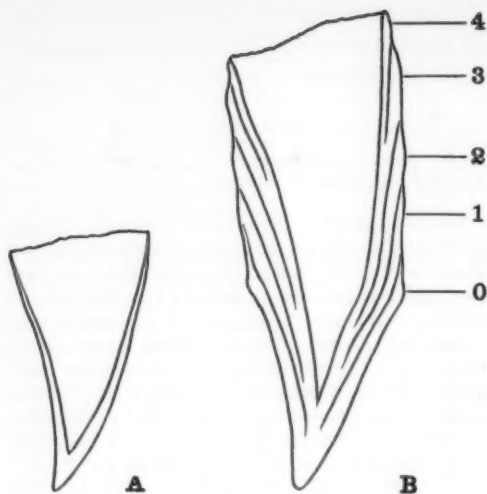


FIG. 1. Teeth of male fur seals, longitudinal section through right upper canines of newborn (A) and 4-year-old (B). Numbers show approximate position of the annual winter growth ridge, with 0 representing the winter of the fetal year. (Twice natural size.)

years corresponded to the number of ridges. This discovery prompted us to ask: "Do growth ridges indicate the true age of a seal, and if so, within what limits of accuracy? Are they present in all members of the Pinnipedia? Why are they found on the teeth of seals but apparently not on the teeth of land mammals?"

At the start of our study we selected the right upper canine, or "fang," of the fur seal as the tooth upon which the growth ridges are most clearly displayed. They are present, however, on all the teeth. When the fur seal young is born in midsummer the canine, as well as most of the other permanent teeth, have erupted. At birth, the crown of the canine is fully developed (Fig. 1). Once erupted, it does not change in size as a result of growth, although it may be reduced through attrition. The crown is covered with a glossy enamel and is marked by a longitudinal keel ending at a minute cusp on the neck, or cementoenamel junction. (The length of the root may conveniently be measured from this cusp.) The root of the tooth increases in length throughout the life of the seal, or at least to the age of senility, a matter of perhaps 20-25 years. The pulp deposits dentine, or ivory, in the root canal until, at an approximate age of 10 years, the canal is completely filled. (The growth of the tooth may be illustrated by stacking cones, one inside the other, each smaller than its predecessor, until a virtually solid object is developed.) Differential deposition of dentine is responsible for the growth ridges visible on the root of the tooth, each representing a winter's growth (Figs. 1, 2).

On canine teeth taken from 75 fur seals of known age, the growth layers accurately represent the age of the individual up to 4 years, and occasionally up to 7 or 8 years, but tend to give false evidence above age 4. On

certain teeth the layers are beautifully displayed, on others barely discernible. The ridge marking the seal's first winter is usually a faint one, an observation in line with the known fact that many members of the yearling class do not return to the Pribilof Islands to rest. Observations of the teeth under ultraviolet illumination give no better results than those under tungsten-filament illumination. Radiographs of entire teeth or of thin sections are, unfortunately, of little value in this connection.¹ The presence of thin layers deposited at intervals of less than a year is one source of confusion, and the extremely variable growth rate among fur seals is another. In mature animals approximately 10 years old and older, the ridges had disappeared—whether by the addition of dentine or by its absorption is not clear.

The differential growth of the tooth root in fur seals is a reflection of an amphibious life. In winter and spring the seals are at sea, spread thinly over the Pacific Ocean from the Aleutian Islands to Southern California. In summer and fall they are on, or adjacent to, the Pribilof Islands. Thus their oceanic pasture and food supply vary markedly from one season to the next. Second, the males tend to abstain altogether from food and drink during the summer season. This is increasingly true with growth and accelerated sexual activity. Prime, breeding males may remain virtually rooted to one station on land for more than 2 months, living on their reserve

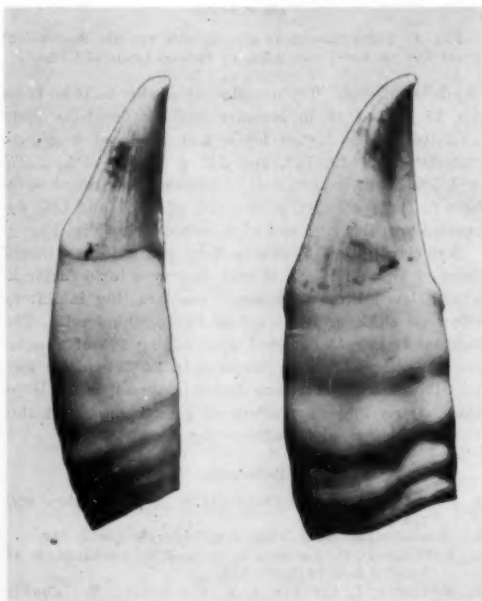


FIG. 2. Teeth of fur seals showing annual growth ridges of 4-year-old male (left) and 7-year-old female (right). (Twice natural size.)

¹ We acknowledge the kindness of B. O. A. Thomas and R. J. Nelsen of the University of Washington School of Dentistry, who prepared radiographs of selected teeth.



FIG. 3. Root of tusk of very old male walrus showing transverse growth ridges that are quite certainly annuli. (One-third natural size.)

fat. Third, the adult females nurse their young in summer for a relatively long period (4 months), during which time the average pup attains a weight one-third to one-half that of its mother. This presumably drains the mother's reserves and retards the growth of her teeth. Growth ridges are evident on the teeth of the female seal, although they are less prominent than on the male.

A brief survey of material in the U. S. National Museum has revealed that growth ridges on the teeth are characteristic not only of the Alaska fur seal but of certain other Pinnipedia as well. (Study of museum skulls is hampered by the fact that in a well-tended collection the teeth are firmly glued in their sockets.) In the family Otariidae, whose members (the fur seals and sea lions) breed on land and form into definite harems, we have observed well-marked rings on the teeth of *Callorhinus*, *Eumetopias*, and *Arctocephalus* and dubious ones on *Zalophus*. In the family Phocidae, whose members (the hair seals and elephant seals), with one exception, breed in the water, we have observed growth rings on an adult female *Phoca vitulina*, but not on certain other species of *Phoca*, *Cystophora*, or *Monachus*. On *Mirotunga*, the elephant seal, which breeds on land and develops a harem structure, the teeth rings are well shown. On one specimen tooth we counted at least 10 rings. In the family Odobenidae, with a single member, the walrus, breeding takes place on land, and a loose harem structure is formed. Tooth rings are present. On a large male walrus tusk lent to us recently, there appear 18 or more evenly spaced rings, the distal ones becoming increasingly faint (Fig. 3). (This tusk, incidentally,

weighs 11 lb, 13 oz, and is apparently the heaviest one on record for North America.)

In practical application to wildlife management research, the growth ridges on the teeth of pinnipeds may be compared to the annuli on certain hard parts of fishes and on the shells of mollusks. Highly specialized techniques have been developed for estimating the age of a fish by means of growth lines on the scales, otoliths, vertebrae, and bony fin rays. A difference may be pointed out, however. The period of rapid growth in seals corresponds to the colder months of the year; in fishes, to the warmer—a logical relationship in view of the fact that fishes adopt the temperature of their environment, and their metabolic rate increases as the temperature of the water rises.

The presence of growth marks on the hard parts (other than teeth) of mammals has been demonstrated by a number of workers. Space does not permit a full account here. Plehanov (*5*), studying the claws of the Greenland seal, found transverse growth ridges that enabled him to estimate the ages of individuals up to 13 years. He was working with specimens of unknown age, however, and was unable to check his conclusions. The claws of the Greenland seal are long and well developed, enabling the owner to crawl about on the floe ice where it spends a good part of its life. The claws of the Alaskan fur seal, however, are used for little else than scratching the body. In this species we have been unable to find growth rings either on fresh claws or on claws treated with boiling NaOH solution. Ruud (*3*) has pioneered a method of estimating the age of a whale by counting selected growth ridges on the baleen plates. Cowan (*1*) has described well-marked annuli on the horns of mountain sheep. Seth B. Benson (in conference) stated that the annuli are especially prominent on sheep from Canada and Alaska, where the difference between summer and winter temperatures is relatively great. We have mentioned the fact that tooth ridges are distinct on the Alaska fur seal and the northern sea lion (*Eumetopias*) but not on the closely related California sea lion (*Zalophus*). This discrepancy is quite possibly a reflection of the north-south temperature gradient in the oceanic environment.

We have examined the *os penis* of the fur seal in the hope of finding evidence of interrupted growth, but, although the bone grows greatly during postnatal life, increasing some 1,500 times in weight, it seems to develop at a steady rate. The possibility is not excluded that growth lines are present and that a technique as yet unexplored will someday reveal them. On logical grounds one would expect to find them.

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Comments and Communications

A Commentary on Structural Variation in Conifer Wood

Sen and Banerjee (*Science*, 1950, 111, 151) have presented x-ray diagrams of the wood of chir pine, both normal and after attacks by *Lensites striata*, from which they claim to show that the fungal infection has led to a change in orientation of the cellulose fibrils in the walls of the tracheids. While rightly pointing out the extreme variability of structure in conifer wood, they are apparently unaware of the systematic study that has been given to it in this laboratory during the past twenty years (Preston, R. D. *Phil. Trans.*, 1934, B 224, 131; *Proc. Roy. Soc.*, London, 1946, B 133, 327; 1947, B 134, 202; *Biochem. et Biophys. Acta*, 1948, 2, 370; Preston, R. D., and Wardrop, A. *Biochem. et Biophys. Acta*, 1949, 3, 585; Wardrop and Preston, *Nature*, 1947, 160, 911). This work makes it desirable to utter a word of warning.

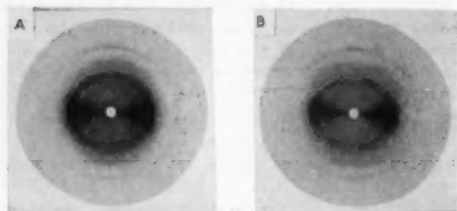


FIG. 1. X-ray diagrams of wood from eleventh annual ring of a specimen of *Pseudotsuga taxifolia*. CuK α radiation, beam perpendicular to grain of wood and along a radius; a, early wood; b, late wood, at a position about 1.5 mm from a. Fig. 1 a compares with Fig. 1 left of Sen and Banerjee, and b with their Fig. 1 right.

An unequivocal demonstration of a change in the sub-microscopic structure of wood after infection would demand a comparison of a sample of infected wood with the same sample before infection, and it is only insofar as the "normal" sample used by Sen and Banerjee duplicates the structure of the "infected" sample before infection that their conclusions can be accepted. It is known that the fine structure of wood varies, not only along the length of a trunk and across the annual rings, but markedly also across a single annual ring. The x-ray diagrams presented here correspond, for instance, to the early wood (Fig. 1, a) and late wood (Fig. 1, b) of the eleventh annual ring of a sample of *Pseudotsuga taxifolia* taken at breast height and are typical of the behavior of conifer wood generally. The difference between these two diagrams is the same in kind, and of at least the same degree, as that shown in the diagrams of Sen and Banerjee. In a block of sapwood of the size used by Sen and Banerjee (4 in. \times 2 in.) there is bound to be considerable structural variation of the kind repre-

sented by their illustrations. Unless, therefore, the irradiated samples of normal and infected wood were chosen with meticulous care, the comparison made between them may well be invalid. Unless, indeed, the two diagrams are examples of many other pairs showing the same difference, it is difficult to see how the claim that a small change in structure is induced by infection could in any case be substantiated.

Even if the difference between the diagrams does correspond to a change in infection and not merely to a normal variation from point to point in the wood, then it is still unsafe to associate it a priori with a change in orientation, whatever that may, precisely, mean. The possibility should not be ignored, for instance, that the fungus may be removing the more disordered fraction of the cellulose with a consequent improvement of the diagram. It is to be suggested that these alternatives—and other possibilities—could best be distinguished by optical investigation of single cell walls under a polarizing microscope. The genesis of the spiral x-ray diagrams would seem to be much too complex for any results of value to be achieved by their further detailed examination by the methods proposed by Sen and Banerjee.

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Maximal Consumption of Ethyl Alcohol

Evidence has recently been advanced by Newman (*Science*, 1949, 109, 594) to show that "the maximum daily consumption of alcohol by a man of average weight is represented by a quart of 100-proof liquor, and that estimates greater than this are in error." This statement has been accepted by the press and by medical authorities (*J.A.M.A.*, 1939, 141, 535) with such a degree of finality that it seems highly desirable to point out certain aspects of this conclusion that have not been previously considered. The establishment of such a figure has many important implications in both medical and legal practice, so that only the most unequivocal evidence should merit such complete acceptance.

It is true, as Newman states, that alcoholics are poor judges of their own alcohol consumption, but there are numerous accounts that indicate that some persons of average weight can consume more than a quart of 100-proof liquor in a 24-hr period, and the writer has himself known two persons who consumed substantially twice this amount over extended periods of time. Newman is certainly correct in asserting that high levels of consumption can only be achieved by maintaining the blood alcohol concentration at a high level, and individuals who consume such large amounts of alcohol are invariably "round-the-clock" drinkers. Both enzyme kinetics and

the greater rate of alcohol loss via excretory channels support the belief that the rate of alcohol metabolism is a function of its concentration in the body. Since the blood alcohol levels upon which certain of Newman's calculations are based are frequently exceeded in actual practice, it follows that higher metabolic rates also occur, and that higher levels of alcohol consumption than those deduced by Newman from the rates of alcohol metabolism quoted by him are therefore possible. It should also be pointed out that, in considering the "maximal consumption" of alcohol, cognizance must be taken of the extreme individual variations in alcohol metabolism that are manifest throughout both the purely experimental and the clinical literature.

It has been shown with rats that consumption of 10% alcohol as a sole fluid source may be less than half their consumption of alcohol under conditions of self-selection (Williams *et al. Arch. Biochem.*, 1949, 23, 275). If this is also true in dogs, as seems likely, then Newman's estimate of the maximum human consumption of alcohol, based on the forced consumption of 10% alcohol by dogs, may be less than half the actual figure. However, many rats on self-selection diets consume amounts of alcohol equivalent to 1,500 ml of absolute alcohol/70 kg man/day without grossly apparent physical effects! This fact suggests grave dangers in assuming that the rate of alcohol metabolism in men and in dogs is the same, for it certainly is not in rats (or in mice). The fact that the basal metabolic rate on a weight basis in dogs is generally about twice that of humans is a reflection of a higher rate of metabolism of many specific substances in dogs, and there is no obvious reason to think that alcohol is not among them. Finally, the fact that the acute oral toxicity of ethyl alcohol for rats (7.4 g/kg) (Welch and Slocum. *J. lab. clin. Med.*, 1943, 28, 1440) is approximately four times that for humans is indicative of a species difference, which in this case follows closely (and perhaps fortuitously) the reciprocal relationship between species size and basal metabolic rate. A number of practical considerations thus suggest that the maximum consumption of alcohol by a man of average weight is at least two quarts of 100-proof liquor, and may even be greater in some cases.

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Textbooks and Courses in General Biology

An unjustifiably harsh review of a textbook of general biology (*The World of Life*, Pauli, W. Houghton Mifflin, 1949) in a recent issue of *SCIENCE* (1950, 111, 368) has raised several fundamental issues relative to the teaching of general biology and the subject matter that should be included in a textbook for such a course. The principal criticisms in the review include: (1) that the book does not instruct in the scientific method; (2) that the author assumes the general biology student has no knowledge of chemistry and physics, and consequently he has a "futile" section in the book on elementary chemistry and physics; and (3) that certain subjects such

as autocatalysis, growth and morphogenesis in terms of chemical and physical changes, and the physicochemical nature of mutations are omitted. These latter subjects, states the reviewer, should be included in a college student's main reading source in biology.

One wonders immediately how the reviewer has managed to give general biology courses only to advanced students. The writer has taught elementary courses in several colleges and universities and has never encountered a class in which the majority had a working knowledge of chemistry and physics. Very few freshmen students have a good background in both these subjects, and many of them take college chemistry and physics in parallel with general biology. In view of these facts and the relatively high percentage of failures in the first-year courses in these physical sciences, it is believed that any author of a general biology textbook is fully justified in assuming that the background of most elementary students in these subjects is slight.

Admittedly, first-year students should have some exposure to the elements of the scientific method, but to what extent this can be successfully taught is certainly a debatable point. It seems to the writer that the scientific method represents a concept that is gradually acquired as one's training proceeds. It is not something that can be unceremoniously stuffed down untrained gullets by requiring the student to read a section in a textbook. Most teachers do not expect a textbook to do all their teaching for them. Indeed, of what value are lecture and laboratory periods if they are not used to give supplementary material? Any elementary textbook that considers detailed scientific experiments and the many failures attendant thereto will very shortly accumulate dust on the bookshelf.

One unfortunate aspect of many textbooks of general biology is the encyclopedic nature of the contents. Apparently the authors feel that more adoptions can be obtained if all imaginable subjects and minute details are included. The text is often not written in an interesting style, and frequently continuity and organization are sadly lacking. As a consequence the average student is soon floundering in a maze of unrelated facts, while he suffers from a bombardment of technical terms. If the present trend continues, many textbooks will be forced off the market, unless the publishers supply special means of transportation for these overgrown biological hodgepodes.

In the writer's opinion, an acceptable textbook for general biology should have certain definite features. It should be from one-half to two-thirds the length of the average textbook available today. It should consider the most important subjects necessary for a good biological foundation, omitting details and many technical terms. It should be written in a readable style and published in an attractive format. Such a book would be adaptable for a wide variety of courses, for any instructor worth his keep can elaborate in lecture or laboratory upon any specific subject that he feels should be emphasized in his particular course.

There are, to be sure, many different kinds of courses in general biology. There are courses designed for spe-

cial groups, such as premedical and pre dental students; others, for the general student who has not committed himself to a definite program of study. Then there is the course that is required of all students who select biology as their natural science subject under certain degree plans. Many institutions have only one course, which is of the latter type. Within this group will be premedics and history majors; students of mathematics and fine arts; boys and girls with extracurricular college "careers"; and individuals who will never be exposed to additional formal work in biology. Last, but not least, we must remember that here are our potential biology majors; we certainly do not wish to discourage them at this stage.

Teachers who have specialized groups, or those connected with institutions that rigidly limit enrollment to students with outstanding high school records, are doubtless justified in covering more material and in giving more details than should be done in the usual course. However, in view of the varied backgrounds and interests of the majority of students, it is believed that courses in general biology should be taught with two fundamental objectives in view: (1) to create an interest in biology, and (2) to give the student a biological background that will serve for future study, and/or help him solve certain problems of everyday life. Such objectives cannot be attained by erudite discourses on autocatalysis, the physicochemical nature of mutation, and morphogenesis in terms of chemical changes. There are enough interesting and worth-while subjects to be introduced without confusing the student with highly technical and controversial issues. It should, of course, be made clear, even to the elementary student, that many unsettled problems in biology do exist, but any detailed consideration should not be undertaken at this stage.

One of the outstanding faults of many young instructors is that they apparently try to impart all their knowledge to their students within a single year. Disillusionment eventually comes to many but, unfortunately, not to all. Obviously the best teachers are in the group in which this does occur.

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May I comment on Ravin's criticism of *World of Life*, by W. F. Pauli?

My own textbook, *Life Science*, had its first edition in 1941, its fourth in 1949. Pauli's text is definitely a

severe competitor, and you might expect me to welcome adverse criticism of it, but, in my considered judgment, the book does not at all warrant Dr. Ravin's condemnation.

Specifically, Dr. Ravin is shocked that Pauli does not stress "growth and morphogenesis in terms of chemical changes; the relation between genes and metabolic processes." He says that these serious faults make it unsuitable for college use, and he relegates it to high schools.

Many of us are alarmed at the utter ignorance of biology exhibited by many, even a majority, of university graduates. It is pitiful to find supposedly highly educated Americans adhering, as they now do, to unsound pseudomedical cults, and believing gross superstitions. This is largely the result of a university curriculum which offers only specialized courses. Biology as advocated by Dr. Ravin will reach extremely few. Do not those who specialize in other fields deserve to know something of geology? Do not they vitally need to know something about biology?

I have taught upper division general physiology, which is a course that delves deeply into such matters as those recommended by Dr. Ravin. We find that for this work the student needs first to have had general inorganic chemistry, then organic chemistry, and preferably also physiological chemistry and general physics, as preliminary studies. All this is fascinating, valuable, but only for specialists in biology. How about the others?

One could teach beginners the relation between genes and metabolic processes, although research specialists realize that they have only begun to understand it themselves. One could teach growth and morphogenesis in terms of chemical changes—but one would then spend so much time in chemical essentials that no time would be left for all the vast field of application of biology to everyday life. Majors in biology would obtain these other items later, in other courses, but how about those who take just one biological course?

An ancient, wise aphorism states that an educated person should know a lot about something, and a little about everything. Texts like those of Dr. Pauli (and mine) contribute toward this, and serve university students well. For this service they should not be abstruse, and therefore Dr. Ravin's condemnation is regrettable.

Can anything be done to balance the scales of justice in such matters?

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Book Reviews

Geochemistry: A Survey of the Chemistry of the Earth.

Kalervo Rankama and Th. G. Sahama. Chicago: Univ. Chicago Press, 1950. 912 pp. \$15.00.

This book is an important contribution to earth science by two eminent Finns, whose broad knowledge of geochemistry is matched by their deep interest in the subject, as shown by the thoroughness with which they have covered the field. An introductory section contains an illuminating discussion of the meaning and proper field of geochemistry. Following Goldschmidt, they believe that this science has for its three objectives the establishment of the abundance of elements and nuclides in the earth; accounting for the manner in which the elements are distributed in the minerals and rocks of the lithosphere and in natural products of whatever kind; and the discovery of the laws governing the relative abundance of the elements.

In discussing the interrelationships and overlapping of mineralogy, geology, chemistry, and geochemistry, the authors dispose of the matter of definition by the wise remark that the definition of geochemistry should not so much involve the subject matter but rather the viewpoint of the scientists attacking its problems. If, for example, the particular subject under consideration is the differentiation by crystallization of a magma, both the petrologist and the geochemist must ordinarily deal with the same basic factors. But the petrologist thinks first of the physical processes involved in differentiation, and the geochemist thinks first of the difference in chemical composition of the various products that are formed. For purposes of orderly treatment, the authors chose to divide the subject matter into two main parts. The first deals with the background and general laws that determine the occurrence and distribution of particular elements; the second treats in detail all the elements in the periodic system in relation to their occurrence.

Although by its name geochemistry has to do with the earth, the first chapter of the book treats of the composition and structure of meteorites, which are interesting in themselves because they supply information on interplanetary and interstellar masses. In addition, they bear directly on geochemistry because, according to general belief, these visitors from outer space represent fragments of a body similar in physical-chemical properties to the earth. The condensed account of the chemical and mineralogical constitution of meteorites, therefore, serves as a useful introduction to the remainder of the book.

Chapter 2 brings together in convenient form information on the abundance of elements and nuclides in the upper silicate layer of the earth (the lithosphere). Succeeding chapters deal with the geochemical structure of the earth, distribution of the elements among the

geochemical spheres of the earth, geochemistry of the lithosphere, geochemistry of the hydrosphere, geochemistry of the atmosphere, and geochemistry of the biosphere. Part I concludes with a chapter on "Cosmochemistry and Geochemistry" and one entitled "Outline of the Geochemical Evolution of the Earth." In these sections, the authors bring together a great variety of facts and theories on cosmogony and the evolution of the earth. Naturally, in a subject such as this, many of the issues are befogged by controversy, but the authors deal fairly and rationally with the divergent views.

In Part II, consisting of 36 chapters, the known elements up to and including atomic number 96 are covered for each element or group of elements under the heads of abundance and geochemical character, the occurrence of the element in rocks, its biogeochemistry, its cycle during geologic processes, and such other heads as may be of importance for the particular element.

The value of this outstanding work is enhanced by a brief historical outline that mentions the milestones and great names in geochemistry, and by some appendices of convenient reference material, such as tables of the atomic and ionic radii of the elements and of the electronic structure of the elements. In addition to literature references and an author index, there is a subject index with over 3,000 listings. The book is clearly written, and the data are presented in convenient form. Typography is attractive, and the book shows evidence of careful preparation, editing, and proofreading. In their preface Rankama and Sahama modestly disclaim any intention to offer here a textbook of geochemistry or a complete account of all geochemical information. Rather, the volume represents an attempt to survey the broad field and to account for the present status of geochemical knowledge. In this purpose they have succeeded admirably, and students of earth science will find this an indispensable reference work.

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Physical Methods in Chemical Analysis, Vol. I. Walter G. Berl, Ed. New York: Academic Press, 1950. 664 pp. \$12.00.

Fourteen competent specialists under the editorship of W. G. Berl contributed to this volume, which represents an impressive piece of work. It renders clear evidence of the continuously increasing importance of physical methods in chemical analysis during the past three decades. Accuracy, convenience, and speed are the characteristics of physical methods that qualify them to supersede older procedures. During the classical period of analytical chemistry, when gravimetric and volumetric methods played the main role, a few physical methods

already enriched the resources of the analyst, but usually many years elapsed between the original conception of a physical method and its introduction into the analytical laboratory. How rapidly nowadays physical methods find application by the analyst is shown by a glimpse at the contents of this volume, which contains all methods dealing with the interaction of radiation with matter.

Three chapters deal with x-rays: "Absorption Phenomena of X-rays and γ -rays," by G. L. Clark; "X-ray Diffraction Methods as Applied to Powders and Metals," by W. L. Davidson; and "X-ray Diffraction as Applied to Fibres," by J. A. Howsmon. These are followed by an article by L. O. Brockway on electron diffraction. "Spectrophotometry and Colorimetry" are presented by W. R. Brode. Three sections are concerned with spectroscopic topics: "Emission Spectrography," J. Sherman; "Infrared Spectroscopy," H. H. Nielsen and R. A. Oetjen; and "Raman Spectra," J. H. Hibben. Polarimetric methods are discussed by C. D. West and "Refractive Index Measurements" by L. W. Tilton and J. K. Taylor. The treatment of "Electron Microscopy" by R. D. Heidenreich emphasizes application to metals. The last article in the volume, written by H. W. Washburn, deals with mass spectroscopy.

All these are excellent monographs about physical methods which are already acknowledged as indispensable means in quantitative analytical work, or will undoubtedly become of steadily increasing importance. Each paper covers the fundamental principles of each field, detailed treatments of methods, clear descriptions of instruments, critical discussions of the various fields of application, and includes a list of references to specialized texts and original research papers. Since all contributors are experts in their special fields, one finds many valuable discussions of a practical nature that could originate only from continuous laboratory experience. There is no doubt that every analyst will greatly appreciate these valuable contributions and will profit from them.

Credit is due to the publishers for the excellent production of this volume.

K. W. MEISSNER

Department of Physics
Purdue University

The Autobiography of Robert A. Millikan. New York: Prentice-Hall, 1950. 311 pp. \$4.50.

Every physicist who has come into contact with Professor Millikan—and who is there of us who has not?—to say nothing of all the countless others in so many fields of practical affairs, will want to read this book in order to discover, if he can, what it is that makes this extraordinary man go. And I believe that he will succeed in finding the answer to a much greater extent than he has a right to expect. It is seldom that a man is so successful in getting his personality into his own writing about himself; here the man we have known speaks to us from every page. Here will be found, for example, an answer to the question which so puzzled or even dis-

mayed the physicists of a generation ago: how was it possible that a man comparatively unheard-of and with no recognized achievement in research should suddenly blossom out at the age of 45 into a physicist of the first magnitude? Although the book does not supply the complete answer, it shows that it was at least no accident. The exuberant energy, and the vision that knew how to concentrate on the essential and the significant, were there all the time, waiting only the inevitable eventual removal of the inhibiting effect of irrelevant and unusual circumstances in his early career.

The book is much more than a record of the life of one man, however; it is a history of the physics of his time, and as such will find its place among the other histories of the most memorable decades that physics has yet experienced.

Not the least interesting part of the book to one who passed through some of the same experiences is the detailed account of Millikan's activities during the first world war. Surely none of the tales of the fabulous activities of physicists during the second war can surpass this tale of its forerunner. But the younger generation should read these war experiences for another reason—as an antidote to the cynicism which became so fashionable in the years immediately after the war. Most of the unselfish men who threw their lives into that war, as did Professor Millikan, were actuated by a sense of high idealism, as were also a large part of the other decent people in this country. This has too easily been forgotten.

P. W. BRIDGMAN

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Harvard University

Heterocyclic Compounds: Three-, Four-, Five-, and Six-Membered Monocyclic Compounds Containing One O, N, and S Atom. Vol. 1. Robert C. Elderfield, Ed. New York: Wiley; London: Chapman & Hall, 1950. 703 pp. \$11.00.

The Chemistry of Heterocyclic Compounds: The Heterocyclic Derivatives of Phosphorus, Arsenic, Antimony, Bismuth, and Silicon. Frederick George Mann. New York-London: Interscience, 1950. 180 pp. \$5.25.

This introductory volume on heterocyclic chemistry proclaims that the series is to be "a general treatment with primary emphasis on the principles involved." This treatise is long overdue, and if the subsequent volumes live up to the high promise of the first volume a long-felt need will be fulfilled. There have been numerous books on heterocyclic chemistry, but the subject is too complex and diverse for one author or one volume. The compendia which tabulate in great detail all available literature on a subject lack critical evaluation of the chemical principles disclosed. The present effort gives promise of fulfilling the need for a chemistry of heterocyclic compounds.

The first volume covers ethylene oxides, trimethylene oxides, ethylenimines, azetes, furans, thiophenes, pyrroles and derivatives, pyrans, pyrones, thiapyrans, thiapyrones, pyridines, partially hydrogenated pyridines, and piperi-

dines. The contributing authors are all well acquainted with their respective fields. If the quality of the sections is not uniform, the variation is due more to available subject matter than to presentation. The more-than-200-page section on pyridines by H. S. Mosher deserves particular comment, since the results in this most prolific field have been amply covered. If any criticism is to be voiced, it is that there is no chapter in which the comparisons of similar ring systems are collected. It may be that later volumes will contain such comments.

Although the type appears to be smaller than average, the typography is good, with adequate leading between the lines. Because of the amount to be compressed into one volume, the reader may experience some eye-strain not encountered in less meaty volumes. The format is excellent, and considering the size, the subject, and the times, the price seems very reasonable.

Arnold Weissberger, as consulting editor, has projected the publication of a 28-volume series covering the field of heterocyclic chemistry, of which this is the first. If the remainder come up to the high standards set by this volume, the series will be a welcome adjunct to any library.

The field of phosphorus, arsenic, antimony, bismuth, and silicon heterocycles is discussed most thoroughly. Attempts are made to correlate the findings from element to element in Group V, with the greatest burden falling on the arsenicals as the best-known of the group. In some instances too much emphasis has been placed on the results obtained by analogy, but in general the presentation is excellent. Some question can be raised as to the use of double bonds in postulating structures with heavier elements, but, since the electronic structure of no compounds of these elements is known with certainty, the question is academic. The electronic interpretations on the whole are good, although frequently they need translation to the American idiom of Pauling, Price, et al. to be completely understood. Dr. Mann is at his best in those instances wherein he has had personal experience, and the contrast in other sections is often striking. Although this results in an unevenness in presentation, it is to be preferred to the uncritical approach of many who review a field of chemistry without knowledge of its particulars. The decision to limit the term "heterocycle" to rings containing at least one carbon is to be regretted, since some of the chemistry thus omitted is admirably suited for inclusion.

In the introduction some of the nomenclature difficulties are discussed. Although the British and *Chemical Abstracts* systems differ, as discussed by Dr. Mann, the discrepancies are even deeper if one examines the German system, or lack thereof. The author wisely selected the *Chemical Abstracts* system as being the more consistent but fails to mention the pitfalls and inconsistencies in this. The nomenclature problem becomes more complex when heterocyclic names are considered. Dr. Mann has done well in following the *Chemical Abstracts* system, which is foreign to him, and only on rare occasion does a British system name occur. German names slip in more frequently, and the *Ring Index* system

is never entirely mastered. The use of the substitutive *area* is abused by making it replace $=CH-$ on occasion and $-CH_2-$ on others. Without prior knowledge of the compounds, some of the ring names would be confusing. Fortunately, structural formulas are used liberally.

References are plentiful, although they are by no means complete. Sufficient source references are given, however, to enable the reader to consult a large portion of the original literature. Typography is excellent and the format good. The addition of biological references makes the book an excellent reference work for those who would acquire a working knowledge of the subject matter. It is to be hoped that the price established on this volume is not indicative of the rest of the series. If so, the more extensive subjects will be beyond all reasonable cost.

C. KENNETH BANKS

Research Laboratory
Metal & Thermit Corporation

Natural Regions of the U.S.S.R. L. S. Berg. Olga Adler Titelbaum, Translator. New York: Macmillan, 1950. 436 pp. \$10.00.

The American Council of Learned Societies has made available in English one of the best books ever written on the natural geography of the U.S.S.R. by encouraging Miss Titelbaum to translate L. S. Berg's *Priroda S.S.S.R.* Although Lev Semenovich Berg's greatest interest was in the field of ichthyology, he published more than 480 books and articles on geology, geobotany, zoogeography, and related subjects. In over 50 years of field work he traveled and did field research in almost every part of the Soviet Union.

Geography has been a well-established discipline in Russia from Czarist days, and Berg's publications and interest in the field made him a leader in the Russian Geographical Society and recipient of many honors and medals. He made a contribution to geographical methodology and theory by his scientific approach to the problem of natural areas. Repeating patterns of the natural phenomena meticulously observed, catalogued, and analyzed finally establish for the U.S.S.R. seven landscape zones for the great lowlands. Berg also establishes twelve mountain landscapes, with varying degrees of vertical zonality.

After the zonal boundaries have been confirmed Berg approaches the areas systematically by a discussion of climate, relief, soils, vegetation, and fauna. Morrison, Nikiforoff, and Miss Titelbaum have carefully checked and supplied both the English and Latin names for the plants and animals. This procedure has enabled the translators to check the Russian and English equivalents with Berg's use of the Latin. About half of the book is devoted to a very clear discussion of the vertical zonations of climates, soils, and vegetation in the mountains in separate parts of the Soviet Union.

We are particularly indebted to Berg for the climatic statistics in both the latitudinal and vertical zones and the discussion of the temperature and precipitation controls on the spread of the various plant associations. One

sometimes wishes for a climatic map of the Soviet Union, but perhaps it is better procedure to combine all the natural features into landscape zones. This may be Berg's greatest contribution to geography and may point the way so that geographers in other areas can limit and divide their studies more sharply into physical and cultural regions; with deeper penetration into each, as Berg has done for the Soviet Union on the physical side.

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Reviewed in Brief

A History of Biology: A General Introduction to the Study of Living Things. Rev. ed. Charles Singer. New York: Henry Schuman, 1950. 579 pp. \$5.00.

All who are interested in the history of science will be glad to see Singer's *History of Biology* revised and back in print. The author's emphasis on biological problems makes his approach stimulating, although his frank dissatisfaction with a mechanistic interpretation of life inserts a bias that numerous readers will deplore. But Singer's scholarship is broad, and adequate to cover a multitude of minor failings, were there such. In general, his treatment of his subject falls between that of Nordenakiöld, which is burdened with detail and over-biased in several respects, and that of Jean Rostand, who excels in presenting the major problems of biology in an up-to-date and most readable way.

Part I of the present book deals with "The Older Biology" and Part II with "The Historical Foundations of Modern Biology"; Part III concerns the "Emergence of Main Themes of Contemporary Biology." These are selective rather than all-inclusive and fail to give a fully rounded picture of modern biology. "Cell and Organism," the "Essentials of Vital Activity," the "Relativity of Functions," "Biogenesis and Its Implications," the "Development of the Individual," "Sex," and the "Mechanism of Heredity" are included, but such fields as endocrinology and biochemistry are represented scantily or not at all. The chief criticism to be made of the book is that its story ends too soon, around 1900 in many fields and around 1920 at the most. Even the "Theory of the Gene," which has been brought up to date better than most sections, lacks a good deal in breadth and perspective. It would be of great assistance to users of the book if the index included subjects as well as personages. In spite of all such limitations, this is a highly worthy book for the shelf of any biologist.

The Practice of Medicine. 5th ed. Jonathan Campbell Meakins. St. Louis, Mo.: Mosby, 1950. 1,558 pp. \$13.50.

In this most recent edition of a well-known textbook of medicine, the author has made a valiant attempt to bring all the chapters up to date. The chapter on the ductless glands has been largely rewritten, and the sparse section of former editions on psychiatry has been

replaced by one on psychosomatic medicine prepared by Frederick R. Hanson. Topics pertaining to the treatment of infections, formerly somewhat scattered throughout the text, have been regrouped in a more logical order under the principles of chemotherapy and antibiotics and the indications and manner of their use.

The book is well bound and its type clearly legible. The numerous illustrations, including 50 in color, have been carefully chosen and effectively complement the clarity of the text. This edition can be heartily recommended as a valuable addition to every physician's library.

Scientific Book Register

Physico-Chemical Constants of Pure Organic Compounds. J. Timmermans. New York: Elsevier, 1950. 693 pp. \$12.50.

Variation and Evolution in Plants. G. Ledyard Stebbins, Jr. New York: Columbia Univ. Press, 1950. 643 pp. \$8.00.

A German-English Dictionary for Chemists. 3rd ed. Austin M. Patterson. New York: John Wiley; London: Chapman & Hall, 1950. 541 pp. \$5.00.

Methods of Mathematical Physics. 2nd ed. Harold Jeffreys and Bertha Swirles Jeffreys. New York: Cambridge Univ. Press, 1950. 708 pp. \$15.00.

A Guide to Psychiatric Books with a Suggested Basic Reading List. Karl A. Menninger. New York: Grune & Stratton, 1950. 148 pp. \$3.50.

The Diagnosis of Salmonella Types. F. Kauffmann. Springfield, Ill.: Charles C Thomas, 1950. 86 pp. \$2.25.

Super-Regenerative Receivers. J. R. Whitehead. New York: Cambridge Univ. Press, 1950. 169 pp. \$4.75.

Radioactivity and Nuclear Physics. 2nd ed. James M. Cork. New York: D. Van Nostrand, 1950. 415 pp. \$5.00.

Electromagnetic Fields: Theory and Applications; Vol I: Mapping of Fields. Ernest Weber. New York: John Wiley; London: Chapman & Hall, 1950. 590 pp. \$10.00.

Melting and Solidification of Fats. Alton E. Bailey. New York: Interscience, 1950. 357 pp. \$7.00.

Electromagnetic Waves. 4th ed. F. W. G. White. London: Methuen; New York: John Wiley, 1950. 108 pp. \$1.25.

Physical Chemistry of High Polymeric Systems. 2nd ed. H. Mark and A. V. Tobolsky. New York-London: Interscience, 1950. 506 pp. \$6.50.

Analytic Geometry. Raymond D. Douglass and Samuel D. Zeldin. New York: McGraw-Hill, 1950. 216 pp. \$2.75.

A Practical Survey of Chemistry. Rev. ed. Walter S. Dyer and Manfred E. Mueller. New York: Henry Holt, 1950. 564 pp. \$3.60.

Physics: A Textbook for Colleges. Oscar M. Stewart. 5th ed. by Newell S. Gingrich. Boston: Ginn, 1950. 726 pp. \$5.00.

Beginning Experimental Psychology. S. Howard Bartley. New York: McGraw-Hill, 1950. 483 pp. \$4.00.

News and Notes

The International Commission of Optics

Stanley S. Ballard

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The second general meeting of the International Commission of Optics of the International Union of Pure and Applied Physics was held in London, July 17-21. Approximately 30 official representatives from Belgium, France, Great Britain, Holland, Italy, Spain, Sweden, Switzerland, and the U. S. attended. The U. S. delegates were I. C. Gardner, National Bureau of Standards, R. Kingslake, Eastman Kodak Company, and S. S. Ballard. No delegates were present from Czechoslovakia or Poland, although these countries have participated in former meetings.

Some of the sessions were diverted to the presentation of progress reports in various technical fields of optics. These reports, prepared by the national committees most concerned, served the useful purpose of bringing interested persons up to date on the progress made in optics since the beginning of World War II. This worthwhile procedure is now substantially completed, and it is not anticipated that the commission will continue this particular activity to any great extent.

The future action of the commission will follow internationally important lines of standardization in optics and will foster colloquies on limited technical subjects. A recommendation for a set of sign conventions and symbols for geometrical optics will be prepared in the hope

that it may find acceptance in various countries. A revised classification for optics, either under the universal decimal system or some other scheme, will be developed. A recommended procedure for the standardization of experimental methods employed in physiological optics will be circulated among the various national committees with a view to facilitating the comparison of data obtained in the laboratories of different countries. An effort will be made to develop a better method of specifying the quality of optical glass.

The need for an all-European optical journal that would do for European optics what the *Journal of the Optical Society of America* does so successfully for American optics was discussed. Much interest was shown in this proposal, despite the realization of the practical difficulties involved in launching such a journal.

Officers elected to administer the affairs of the commission until its next general congress were: president, A. C. S. van Heel, of the Technical University of Delft, Holland; vice presidents, L. C. Martin, of Imperial College, London; J. M. Otero, of the Optical Institute Daza de Valdes, of Madrid, Spain; and S. S. Ballard of Tufts College, Medford, Massachusetts. P. Fleury and A. Arnulf, both of the Institut d'Optique of Paris, will continue to serve as secretary and treasurer, respectively.

About People

Callaway Brown, an authority on luminescent and electronic materials, has been named research physical chemist at Armour Research Foundation of Illinois Institute of Technology. Dr. Brown has been a research associate with General Electric Company, Schenectady, N. Y., since 1945.

Harry J. Olausen, formerly of the School of Medicine, the University of Arkansas, has joined the Department of Anatomy at the University of South Dakota, School of Medicine, as associate professor.

John E. Funnell, formerly research ceramist with Corning Glass Works, has been appointed ceramics engineer and economic geologist for Southwest Research Institute, San Antonio, Texas. Dr. Funnell will

take part in the institute's program of research in industrial minerals.

R. F. Rinehart, former executive secretary of the Research and Development Board, will resume his position as professor of mathematics at the Case Institute of Technology.

Edward J. Schwoegler, former technical director of Nox-Rust Chemical Corp., Chicago, has joined the staff of Armour Research Foundation of Illinois Institute of Technology as a research organic chemist.

Indiana University's Department of Bacteriology has appointed **J. L. Stokes** as associate professor, and **Emilio Weiss** and **Eugene D. Weinberg**, formerly of the Department of Bacteriology and Parasitology, University of Chicago, as assistant

professor and instructor, respectively. Dr. Stokes is completing three years' work as research associate at the Hopkins Marine Station, Pacific Grove, Calif.

John A. Waters, Jr., Captain (USN), has been appointed director of the Division of Security of the U. S. Atomic Energy Commission. Captain Waters succeeds **John E. Gingrich**, Rear Admiral (USN), who resigned in May, 1949. **Francis Hammack**, formerly chief of the Personnel Security Branch, has been acting director of the division since that time.

Emil Witschi, of the Zoology Department, State University of Iowa, has been elected to honorary membership in the Société Zoologique de France.

Visitors

Speakers at the 8th annual Pittsburgh Conference on X-Ray and Electron Diffraction, to be held at the Mellon Institute in Pittsburgh, November 2-3, include **O. Kratky**, University of Graz, Austria, **A. Guinier**, **G. Fournet**, and **D. Derivichian**, Conservatoire National des Arts et Métiers, and **Yvette Cauchois**, Laboratoire de Chimie Physique, Université de Paris, Paris, France.

Recent visitors at the National Bureau of Standards were: **Harald Bergstrom**, professor of applied mathematics, Chalmers University of Technology, Gothenburg, Sweden; **Leslie Fox**, Mathematics Division, National Physical Laboratory, Teddington, England; **Genji Furusho**, chief electrical engineer, Engineering Section, Bureau of Industry, Tokyo; **Shigenori Hamada**, professor of electronics at Tohoku University in Sendai, Japan; **Ichiro Itaka**, president of the Casting Institute of Japan, and professor of metallurgy at Waseda University; **Clement J. Tranter**, associate professor of mathematics, Military College of Science, Shrivenham, England; **B. K. Vaidya**, assistant director, Ahmedabad Textile Industry's Research Association, Ahmedabad, India; and **Shikao Ikehara**, head, Department of Mathematics, Tokyo Institute of Technology.

The National Bureau of Standards was host last month to **S. Luthander**, professor of aeronautics, Division of Aeronautics, Royal Institute of Technology, Stockholm, and **Luis A. Asorio Struve**, Faculty of Engineering, Universidad Central, Caracas, Venezuela.

Grants and Awards

Research Corporation has allocated nearly \$250,000 in the form of 83 grants-in-aid of research to colleges, universities, and scientific institutions in 24 states and the District of Columbia. The awards, which include both Research Corporation General Grants and Frederick Gardner Cottrell Grants to smaller institutions, bring to a total of about \$550,000 the funds granted since

November 1, 1949. Of the 64 Frederick Gardner Cottrell grants, 31 are renewals on projects already being supported by foundation funds, and 33 are new grants. Nineteen General Grants were made, including new grants and renewals. The new grants are: University of Arizona—**Edward J. Meyer**, equilibria of artificial mineral phases in silicate melts; University of Arkansas—**E. S. Amis**, study of dielectric constant and temperature dependence of equivalent conductance of electrolytes at infinite dilutions; Occidental College—**Frank L. Lambert**, factors influencing the polarity of halogens in organic chemistry; University of San Francisco—**Arthur Furst**, the chemistry of organic phosphorus compounds; University of Southern California—**Donald W. Visser**, synthesis and biological activity of purine and pyrimidine nucleoside; Whittier College—**Robert P. Kraft**, light curves of typical Cepheids in various colors; George Washington University—**William F. Sager**, synthesis of ketotriazines and studies on reactions of iodine radicals; Howard University—**R. Percy Barnes**, study of the structure of isoxalines, isoxaxoles, alpha- and beta-diketones by means of infrared spectroscopy; University of Idaho—**James F. Murphy**, electrical behavior of simple inorganic salts in nonaqueous solutions; De Pauw University—**Howard Burkett**, reactions of 1,1,1-trichloro-3-nitropropanol-2; Indiana University—**R. W. Thompson**, the high energy nuclear interactions of cosmic rays; Wabash College—**Clayton M. Ziemann**, dielectric constants of gases at wavelengths of approximately 3 centimeters; State University of Iowa—**Charles Tawford**, ionization of phenolic hydroxyl groups in proteins; Amherst College—**George W. Kidder**, a study of metabolic inhibitors as chemotherapeutic agents in the control of cancer and viral invasions; Tufts College—**Fred L. Greenwood**, a quantitative study of the ozonization reaction; University of Massachusetts—**Gilbert L. Woodside**, chemotherapeutic studies on cancer in mice; Kalamazoo College—**Laurence E. Strong**, small ion-protein interactions as determined by electrical conductivity; University of Michigan—**Charles L. Rulfs**, oxidation levels of

rhodium in aqueous media; Carleton College—**John E. Baer**, some reactions of 2-imidazolinethione; Missouri School of Mines and Metallurgy—**M. E. Straumanis**, an investigation by x-ray methods of the expansion coefficients of compounds showing metallic properties; Princeton University—**E. Newton Harvey**, biochemical studies of luminous substances from the crustacean, *Cypridina*; Canisius College—**Robert H. Schuler**, radioiodine as a free radical detector for liquid phase process; Columbia University—**Benjamin P. Dailey**, application of microwave spectroscopy to chemical problems; Columbia University—**Harvey Fletcher**, research in musical acoustics; Pratt Institute—**George B. Diamond**, the electrolytic reduction of some substituted naphthalenes; University of Rochester—**Seymour L. Friess**, the reaction of organic peracids with ketones and with polysubstituted aromatic systems; University of North Carolina—**Oscar K. Rice**, photolysis of azoethane; Antioch College—**I. Moyer Hunsberger**, use of infrared spectra in determining the degree of bond fixation in polycyclic systems; Kenyon College—**Eric S. Graham**, the rearrangement of alpha halo-ketones under the influence of silver nitrate; University of Cincinnati—**Alvin A. Kosak**, the chemistry of hydroxythiophene derivatives; Bucknell University—**Charles A. Russell**, a new instrument for measuring magnetic susceptibilities; Pennsylvania State College—**Ray Pepinsky**, crystal structure of the ergot alkaloids; Pennsylvania State College—**James J. Frits**, an investigation of the magnetic and thermodynamic properties of paramagnetic salts below 4 degrees Kelvin; University of Pennsylvania—**Melvin C. Molstad**, pressure drop in vertical tubes in the transport of solids by gases; North Texas State College—**Price Truitt**, study of cleavage of 1,1-di-(2-thienyl) alkanes with Raney nickel both with and without added hydrogen; The Rice Institute—**William D. Walker, Jr.**, a cloud chamber study of penetrating showers; Southern Methodist University—**Ogden Baine** and **Harold Jeskey**, study of the Kolbe-Schmitt reaction; Virginia Polytechnic Institute—**Dan H. Pletta**, analysis of skewed rigid

frame bridges; Saint Martin's College—*F. E. Horan*, ultrasonic investigations of solutions of starches, starch fractions, and starch derivatives; State College of Washington—*Carl J. Nyman*, electrochemical reduction of quaternary ammonium salts at mercury cathodes; and Beloit College—*F. J. Mathews*, further cyclization studies in the benzoquinoline series.

Laurent Schwartz, University of Nancy, France, and Atle Selberg, a permanent member of the Institute for Advanced Study, Princeton, N. J., were awarded **Fields Medals** at the opening session of the International Congress of Mathematicians, August 30, at Harvard University. The Fields Medals are named for J. C. Fields, of the University of Toronto, who was president of the 1924 congress held in Toronto, Ontario.

Fellowships

The American Society for the Study of Sterility offers an annual award of \$1,000, known as the **Ortho Award**, for an outstanding contribution to the subject of infertility and sterility. Competition is open to those in clinical practice as well as persons whose work is restricted to research in the basic sciences. Essays submitted for the 1951 contest must be received not later than **March 1, 1951**. The prize essay will appear on the program of the 1951 meeting of the society. For particulars, address the American Society for the Study of Sterility, 20 Magnolia Terrace, Springfield, Mass.

E. I. du Pont de Nemours & Co. is offering 76 postgraduate and post-doctoral fellowships in chemistry, physics, metallurgy, and engineering, for the academic year 1950-51. The selection of candidates for the fellowships and the choice of problems on which they are to work will be made by the 47 universities that receive awards. The stipend for the 70 postgraduate fellowships is \$1,200 for a single person and \$1,800 for a married person. The six post-doctoral fellowships, for work in chemistry, provide \$3,000 to the recipient. The latter fellowships are

designed to serve as an incentive to individuals who wish to enter industrial research work as well as those who prefer to remain in academic work. Further information about the program can be obtained from the Du Pont Company, Wilmington 98, Del.

The Marine Biological Laboratory, Woods Hole, Mass., through a grant from the Lalor Foundation, is offering a limited number of post-doctoral fellowships in the fields of biochemistry, biophysics, and physiological chemistry. The fellowships are designed primarily for young scientists desiring* to work the entire summer on investigations for which the opportunities provided by the laboratory are particularly appropriate. The stipend is intended to cover laboratory fees, travel, and living expenses at Woods Hole. Applications should be received by **December 31**. Blanks and further information may be secured from the director of the laboratory.

Colleges and Universities

A virus laboratory unit has been established in the Department of Bacteriology, **University of Illinois College of Medicine**, to train virologists and to maintain a full program of research. Several investigations already have been undertaken, with the support of the U. S. Public Health Service, the university's Graduate College, and Eli Lilly and Company, Indianapolis. Under the direction of John E. Kempf, research is now being conducted, using the electron microscope, on the virus etiology of certain skin diseases.

Ohio State University will establish an Institute of Genetics to coordinate current research programs in genetics and to foster new studies in several departments and colleges of the university. It will also coordinate instructional programs at both the undergraduate and graduate levels. Chairman of the governing body of the institute will be D. C. Rife, of the Department of Zoology and Entomology.

Richard S. Crutchfield will spend a second year as a visiting professor

in the Department of Psychology of the **University of California at Berkeley**. W. C. H. Prentice will continue as acting chairman of the Department of Psychology at Swarthmore College in Dr. Crutchfield's absence. Wolfgang Köhler will spend the first semester on leave from Swarthmore as visiting professor at the University of Chicago.

An Institute of Human Biology has been organized at the **University of Michigan** to direct the operations of the Heredity Clinic, the Laboratory of Vertebrate Biology, and related projects. Lee R. Dice, former director of the Laboratory of Vertebrate Biology, is the director of the new institute.

Industrial Laboratories

General Biochemicals has published its August catalogue listing 224 special products for investigational use in the fields of biology, microbiology, bacteriology, biochemistry, and nutrition. Types of products included are amino acids, carbohydrates, nucleoproteins, purines, pyrimidines, enzymes, microbiological and bacteriological media, complete biological test diets, various test diet ingredients, and miscellaneous research biochemicals. Copies of the catalogue are available on request to General Biochemicals, Inc., Laboratory Park, Chagrin Falls, Ohio.

Sharp & Dohme has entered into a contract with the Armed Services Medical Procurement Agency to construct additional blood plasma processing facilities at West Point, Pa. Sharp & Dohme will build the structure required, and the Army will provide the equipment for the lyophilization process, which makes it possible to use plasma stored for as long as 5 years.

Kodak Limited, London subsidiary of Eastman Kodak Company, has appointed Douglas A. Spencer as a deputy managing director. Dr. Spencer, a specialist in photographic consulting work, has been technical advisor to the chairman of the board of directors since 1945.

The Will Corporation, distributors of laboratory equipment and supplies, has acquired its fifth division with the purchase of the business of E. J. Callahan & Co., of Baltimore, and will operate it under the name of Will Corporation of Maryland. Will, founded in 1919, also operates office-warehouses in Rochester, New York City, Buffalo (the Buffalo Apparatus Corp.), and Atlanta (the Southern Scientific Company). The Baltimore division will serve Maryland, Delaware, and the District of Columbia.

The 1950 edition of *Laboratory Apparatus and Reagents* has just been published by the **Arthur H. Thomas Company**. It lists 15,342 items of apparatus, with 5,401 illustrations, and 2,570 reagent items, in 6,289 types of packages, all primarily for use in chemistry and biology laboratories. A comprehensive index of 62 pages is included. Many complete assemblies for specific tests are listed, particularly for use in the field of microchemistry; variations to suit individual requirements are also available. Information about the catalogue may be obtained from Arthur H. Thomas Company, 230 South Seventh Street, Philadelphia 5.

Meetings

Progress and New Developments in Antibiotics will be the subject of a lecture seminar to be held this fall in the U. S. Department of Agriculture Administration Building, Washington, D. C., under the sponsorship of the USDA Graduate School. The course will be directed by George W. Irving, Jr., assistant chief, and Thomas D. Fontaine, head, Biologically Active Chemical Compounds Division, Bureau of Agricultural and Industrial Chemistry, USDA. The registration fee is \$18. Classes will meet from 6:00 to 8:00 P.M. in the USDA Administration Building, 14th and Independence Avenue, S.W., Washington, D. C. Dates and lecturers are as follows:

Sept. 25—Monroe J. Romansky, George Washington University Medical School

Oct. 2—Kenneth B. Raper, Northern Regional Research Laboratory, USDA

Oct. 9—Loren M. Long, Parke, Davis & Company

Oct. 16—Robert D. Coghill, director of research, Abbott Laboratories

Oct. 23—Gladys L. Hobby, Charles Pfizer & Company

Oct. 30—B. M. Duggar, Lederle Laboratories Division, American Cyanamid Company

Nov. 6—(Speaker to be announced)

Nov. 13—Thomas D. Fontaine and George W. Irving, Jr.

Nov. 20—Harry Eagle, Microbiological Institute, National Institutes of Health

Nov. 27—Henry Welch, Division of Antibiotics, Food and Drug Administration

Dec. 4—H. R. Bird, Bureau of Animal Industry, USDA

Dec. 11—John R. Majchett, Bureau of Agricultural and Industrial Chemistry, USDA

Dec. 18—A. F. Langlykke, director of research, E. R. Squibb & Sons

Jan. 8—Joseph E. Smadel, Department of Virus and Rickettsial Diseases, Army Medical Center

Jan. 15—Selman A. Waksman, Rutgers University

Further information may be obtained from Harold F. Eisele, Assistant Director, USDA Graduate School, Washington 25, D. C.

The annual field meeting of the **New England Intercollegiate Field Geologists** will be held October 14-15, in the Bangor, Maine, region, under direction of Joseph Trefethen, University of Maine. For further information write Lloyd W. Fisher, 41 Central Avenue, Lewiston, Maine.

The **32nd National Metal Congress and Exposition** will be held in Chicago, October 23-27. Sponsored by the American Society for Metals, American Welding Society, Metals Institute Division, American Institute of Mining and Metallurgical Engineers, and Society for Non-Destructive Testing, the congress will bring together the metal-working industry's knowledge of materials, processes, and equipment, through demonstration, conference, forum, lecture, and clinic, for evaluation on the basis of its most effective use with materials, plants, and equipment. Approximately 350 firms engaged in the production of metals, the treatment of metals, their fabrication, or in rendering services to all these, will exhibit their products, equipment, or services in Chicago's International Amphitheatre. Spe-

cial events will be the American Society for Metals Business Forum, the A.S.M. Sales Clinic, industrial motion pictures, and technical sessions.

Final dates for the **Third Annual Joint Conference on Electronic Instrumentation in Nucleonics and Medicine** of the American Institute of Electrical Engineers and the Institute of Radio Engineers have been set as October 23-25. Location of this meeting, which will feature technical papers and discussions on the various problems in instrumentation for the vital fields of nuclear and medical science, is the Park Sheraton Hotel, New York City.

A Conference on **What Is the Scientific Method?** will be held at Roosevelt College in Chicago, October 21-22. The conference, sponsored by the college in cooperation with the Philosophy of Science Association, will investigate the experimental techniques responsible for the rapid gains of science and methods by which they may be used to stimulate social progress. Sessions of the conference will be led by Sebastian Littauer, chairman of the Department of Mathematics at Columbia University; Nicholas Rashevsky, chairman of the Committee on Mathematical Biology at the University of Chicago; Howard Becker, professor of sociology, University of Wisconsin; and Thomas Cowan, professor of law, Wayne University. Edward J. Sparling, president of Roosevelt College, will deliver the opening address.

The 35th annual meeting of the **Optical Society of America** will be held at the Hotel Statler, Cleveland, October 26-28. Papers covering all phases of optics will be presented. On October 27 the society will be the guest of the General Electric Company at Nela Park. Arrangements are also being made for a trip to the Case Observatory on October 26, at which time J. J. Nassau, of the Case Institute of Technology, will speak on "Schmidt Optics in Astronomy." The meeting will be open to nonmembers of the society, and all interested persons are invited to attend. Further informa-

tion may be obtained from Arthur C. Hardy, Secretary, Optical Society of America, Massachusetts Institute of Technology, Cambridge 39, Mass.

The American Institute of Chemical Engineers will hold its 43rd annual meeting December 3-6 at the Neil House and the Deshler-Wallick Hotel in Columbus, Ohio. The program will include symposia on air pollution, glass manufacture, ultrasonics, the processing of viscous materials, and phase equilibria. For details concerning reservations and registration, address S. L. Tyler, Executive Secretary, American Institute of Chemical Engineers, 120 East 41st Street, New York City 17.

The following officers were elected at the meeting of the **American Society of Ichthyologists and Herpetologists**: John Treadwell Nichols and Helen T. Gaigo, honorary presidents; George S. Myers, president; Robert C. Stebbins, Frederick H. Stoye, and Fred R. Cagle, vice presidents; Edward C. Raney, secretary; N. B. Green, publications secretary; and Dwight A. Webster, treasurer.

The Society of American Foresters will hold its 50th anniversary meeting at the Mayflower Hotel,

Washington, D. C., December 13-16, in commemoration of the founding of the organization in 1900. In addition to general sessions, subject divisions will hold meetings on private forestry, forest economics, forest recreation, forest products, forestry education, forest-wildlife management, silviculture, public relations, and watershed management. Information about the meeting may be obtained from the society's headquarters, 825 Mills Building, Washington, D. C.

Miscellaneous

The World Health Organization, which already has set up regional organizations in the Eastern Mediterranean area, Southeast Asia, and the Americas, as well as a special office for Europe, is now preparing for the creation of a new regional organization for the Western Pacific area. The region provisionally includes Australia, China, the Philippines, South Korea, New Zealand, Viet Nam, Laos, Cambodia, Japan, Malaya, and Singapore, comprising over 600 million people. Although the separate organization is new, the agency has already worked in the region in fields ranging from

campaigns against malaria, tuberculosis, and venereal diseases to the training of nurses and surgeons. The Philippines was the first to ask WHO for aid in setting up a mental health system throughout its territory. A consultant was sent from Geneva to help establish a mental health program, including child guidance clinics. Other Western Pacific territories that have benefited from WHO assistance are Australia, China, Hong Kong, Malaya, Singapore, North Borneo, Brunei, Sarawak, South Korea, Indonesia, and New Zealand.

A chronic disease research institute has been established in Buffalo as a joint project of the U. S. Public Health Service, the New York State Department of Health, and the University of Buffalo's Medical School. The new institute plans a 50-bed inpatient service for research in specific problems of chronic disease. The out-patient service will include a unit for physical rehabilitation, a multiple screening unit, and a rehabilitation center for chronic alcoholics.

The American Council of Voluntary Agencies for Foreign Service is providing clearinghouse services to persons or organizations who wish to dispose of their bound volumes of medical journals. The council, through its American member agencies, coordinates plans and activities with nonmember agencies, and with governmental and intergovernmental agencies in the U. S. and abroad, to provide relief for war-stricken peoples. Further information can be obtained from the council at Willkie Memorial Building, 20 West 40th Street, New York City 18.

A new publication, *Journal of Atmospheric and Terrestrial Physics*, will soon be published by Butterworth-Springer, London. Edited by Sir Edward Appleton, secretary of the Department of Scientific and Industrial Research, the publication will appear every two months. The cost per volume is \$10.

A panel on environmental cancer has been formed by the Committee on Growth of the National Research



Architect's elevation of the new 22-story, \$12,000,000 Mayo Memorial Center now under construction at the University of Minnesota. When it is completed sometime in 1953, it will serve as a memorial to the Drs. Mayo. Funds for construction came from private donors, Federal agencies, the Minnesota state legislature, and from various medical research foundations and agencies.

Council, advisor for research to the American Cancer Society. The new panel, with William Machle as chairman, will be concerned with the status of knowledge in this field and with criteria for the establishment of valid relationships between environment and occupation and the occurrence of cancer. The panel will also review applications for grants in support of research on environmental factors in cancer; applications will be received until October 1. Communications regarding grants may be addressed to the Executive Secretary, Committee on Growth, National Research Council, 2101 Constitution Ave., Washington 25, D. C.

Staff members of the 48th expedition of the Department of Tropical Research of the New York Zoological Society recently returned from a six-month stay in the northern mountains of Trinidad. The expedition was under the direction of William Beebe, director of the Department of Tropical Research of the society. Headquarters were at Simla, a 200-acre estate in the Arima Valley, purchased as a field laboratory. Another expedition to Simla will leave early next year.

Genetics—The Science of Heredity, a popular interest pamphlet on genetics, was published on September 11 by the Genetics Society of America. The text, written by John Pfeiffer, science director of Columbia Broadcasting Company, give the story of genetics in popular terms, and should be of special value to teachers, science students, farmers, doctors, and adult study groups. It records the contributions of Mendel, describes the place of genetics in the life sciences, explains results of applied genetics in agriculture, medicine, and other fields, and reports the case of the Russian renunciation of Mendelian principles. Copies may be ordered from Public Affairs Committee, 22 East 38th Street, New York City 16, for 20 cents a single copy. Discounts are available on larger quantities.

The Registry of Rare Chemicals, 35 West 33rd Street, Chicago 16, list the following wanted chemicals strontium tartrate tetrahydrate;

aluminum triethyl; 2-carboxy-5- α -butyl pyridine; 1,5-dimethyl imidazole; 1,5-dimethyl iminazole; D- or L-ethyl lactate; 1-methyl-5-cyano-methyl imidazole; tetramethylhydrazine; 3-hydroxy-N-methylmorphinan; 1-(p-methoxyphenyl)-1,2-epoxypropane; N,N-dimethylthioacetamide; 4-amino-2-carboxy-1-N-phenyl-4-amino-4'-oxy-1,1'-diphenylmethane; 2-amino-5-nitrothiazole; 2- α -butyl hydroquinone; triethoxychlorosilane; carvacrol, pure; emodin; fraserin; and phytolaccinum.

Pharmacological Basis of Penicillin Therapy, by Karl H. Beyer, director of pharmacological research, Sharp & Dohme, has been published by Charles C Thomas Co., Springfield, Ill. Of special interest to clinicians, medical students, pharmacologists, and general practitioners, the book contains 37 illustrations and 200 pages of practical information organized for easy reference. In addition to the monograph, the text contains an addendum summarizing the preclinical information and clinical indications for "Benemid," an enzymological compound discovered since Dr. Beyer's book went to press. The book represents the first in a series of "American Lectures in Pharmacology," edited by Chauncey D. Leake, vice president in charge of medical affairs, University of Texas.

Cooperative Determinations of the Amino Acid Content, and of the Nutritive Value of Six Selected Protein Food Sources has been issued by the Bureau of Biological Research of Rutgers University. The studies were carried on during 1946-50 by 32 laboratories in 11 universities and in 13 industrial organizations. Sixteen amino acids in each of the six protein sources were determined by several methods, all using the same standards distributed by the bureau. Nutritive values for growth, maintenance, regeneration, reproduction, and lactation were determined for each protein source, also distributed by the bureau. Species used were chick, mouse, rat, dog, and man. Copies of the report may be obtained at \$1.50 each by writing William H. Cole, Rutgers University, New Brunswick, N. J.

Recently Received—

Name Index of Organic Reactions.

T. S. Wheeler and J. E. Gowan. Society of Chemical Industry, 56 Victoria Street, London, S.W. 1. 5s.

Acceptance Sampling: A Symposium.

The American Statistical Association, 1603 K Street, N.W., Washington, D. C.

Baltic Amber Spiders in the Museum of Comparative Zoology.

Alexander Petrunkevitch. Bull. 5, Vol. 103. Museum of Comparative Zoology, Harvard College, Cambridge, Mass.

Arthritis and Rheumatism Foundation: Annual Report, May 1, 1949 to April 30, 1950.

535 Fifth Avenue, New York City.

Expert Committee on Malaria: Report on Third Session.

World Health Organization, Tech. Rep. Series No. 8. WHO, Palais des Nations, Geneva. 30 cents.

Ecological Crop Geography of Finland and Its Agro-Climatic Analogues in North America.

M. Y. Nuttonson. American Institute of Crop Ecology, P. O. Box 1022, Washington, D. C.

Weather and the Building Industry: Proceedings of Research Correlation Conference, January 11-12, 1950.

Building Research Advisory Board, Division of Engineering and Industrial Research, National Research Council, Washington 25, D. C.

Poisonous Fishes of the South Seas.

Special Scientific Report: Fisheries No. 25. Fish and Wildlife Service, U. S. Department of the Interior, Washington 25, D. C.

Abridged Scientific Publications.


Vol. 30. Eastman Kodak Company, Rochester, N. Y.

Behaviour of Swarm Hoppers of the Australian Plague Locust Chortocetes terminifera (Walker).

L. R. Clark. Bull. 245, Commonwealth Scientific and Industrial Research Organization, Melbourne, Australia.

Supply and Demand for Geologists.

Report of Committee on Geological Personnel, American Geological Institute. National Research Council, 2101 Constitution Avenue, Washington 25, D. C.



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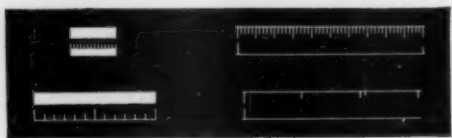
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STATISTICAL DECISION FUNCTIONS

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By LAWRENCE E. KINSLER and AUSTIN R. FREY, *U. S. Naval Postgraduate School*. A solid treatment of basic facts about the generation, transmission, and reception of acoustic waves. Its aim is to orient the reader in fundamentals and terminology, and in analytical methods for attacking acoustical problems. The first half analyzes types of vibration in solid bodies, and the propagation of sound through fluid media. Then such applications are covered as loudspeakers, microphones, psychoacoustics, architectural and underwater acoustics, and ultrasonics. October. 516 pages. Prob. \$6.00.

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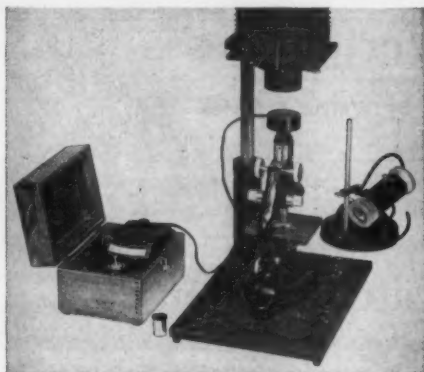
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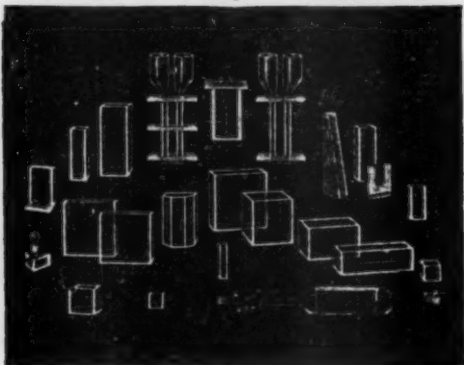
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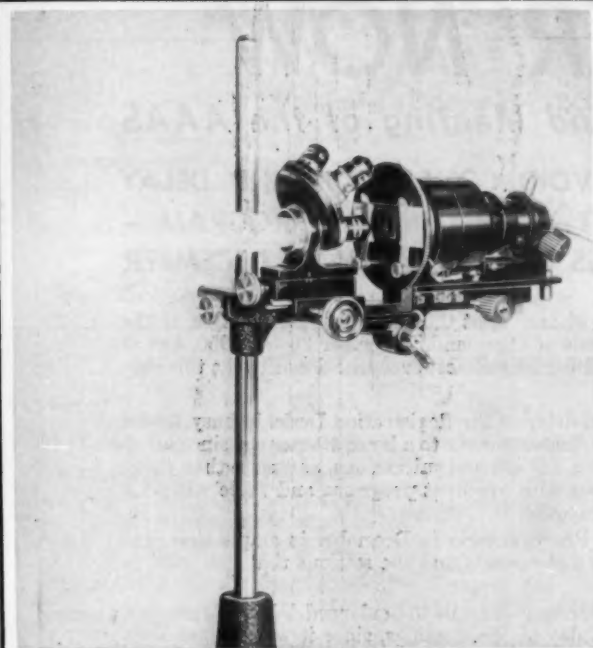
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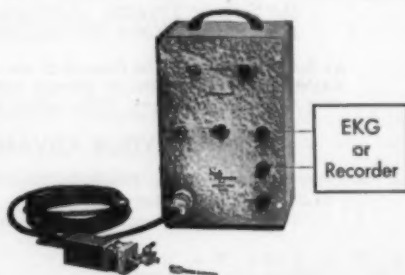
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☐ \$2.25 Wife (or Husband) of Registrant ☐ \$3.25 Nonmember of A.A.A.S.
2. FULL NAME (Miss, Mrs., Dr., etc.) _____
(Please print or typewrite) (Last) (First) (Initial)
3. ACADEMIC, PROFESSIONAL, OR
BUSINESS CONNECTION _____
4. OFFICE OR HOME ADDRESS _____
(For receipt of Program and Badge)
5. YOUR FIELD OF INTEREST _____
6. CONVENTION ADDRESS _____
(If not known now may be added later)
7. DATE OF ARRIVAL _____ DATE OF DEPARTURE _____

Please mail this Coupon and your check or money order for the fee, \$2.25 or \$3.25, to
AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE
1515 Massachusetts Avenue, N.W., Washington 5, D. C.

HOTEL RESERVATIONS

117th AAAS MEETING

Cleveland, December 26-30, 1950

The list of hotels and the reservation coupon below are for your convenience in making your hotel room reservation in Cleveland. Please send your application, *not* to any hotel directly, but to the Housing Bureau of the Cleveland Convention and Visitors' Bureau to avoid delay and confusion. The experienced Housing Bureau will make assignments promptly and the hotel will send a confirmation directly to you in two weeks or less. **Please plan to share a room with a colleague.** In addition to economy, this will insure ample accommodations for all in the *downtown* hotels. Mail your application *now* to secure your first choice of desired accommodations.

HOTELS AND RATES PER DAY

Hotel*	Single	Double	Twin-Bedded	Suites
STATLER	\$4.00-\$8.00	\$7.00-\$10.00	\$8.50-\$12.50	\$17.00-\$23.00
HOLLENDEN	\$3.50-\$8.00	\$5.50-\$10.00	\$7.00-\$12.00	\$12.00-\$22.00
CARTER	\$4.00-\$6.50	\$6.00-\$10.00	\$7.00-\$10.00	\$18.00-\$25.00
ALLERTON	\$3.50-\$7.00 \$2.50 RW	\$6.00-\$ 9.00	\$6.00-\$10.00 \$4.00 RW	\$10.00-\$20.00
AUDITORIUM	\$3.50-\$5.00	\$5.50-\$ 7.50	\$7.50	\$12.50-\$26.00
OLMSTED	\$3.00-\$6.00	\$5.00-\$ 9.50	\$7.00-\$ 9.50	\$10.00-\$15.00

Prices are subject to change, but are not likely to do so.

RW means running water only—no private bath.

* A list of the headquarters of each society and section is under **Association Affairs, SCIENCE**, August 25 and in **THE SCIENTIFIC MONTHLY** for September.

THIS IS YOUR HOTEL RESERVATION COUPON

Mrs. Louise D. Perkins, Director
Housing Bureau
Cleveland Convention and Visitors' Bureau, Inc.
511 Terminal Tower
Cleveland 13, Ohio

Date of Application

Please reserve the following accommodations for the 117th Annual Meeting of the AAAS:

TYPE OF ACCOMMODATION DESIRED

Twin-Bedded.....Rate.....
Suite.....Rate.....Number in Party.....
Double Room.....Rate.....
Single Room.....Rate.....Sharing this room will be:
.....persons

(Enumerate and attach list giving name and address of each person, including yourself)

CHOICE OF HOTEL

First Choice.....Second Choice.....Third Choice.....

DATE OF ARRIVAL.....DEPARTURE DATE.....

(These must be indicated)

SIGNED.....

(Please print or type)

ADDRESS.....

(Street)

(City and Zone)

(State)

Mail this now to the Housing Bureau.

Rooms will be assigned and confirmed in order of receipt of reservation.

Hotels will confirm directly in two weeks or less.

Personnel Placement

CHARGES and REQUIREMENTS for "PERSONNEL PLACEMENT" Ads

1. Rate: 15¢ per word, minimum charge \$3.00 for each insertion. If desired, a "Box Number" will be supplied, so that replies can be directed to SCIENCE for immediate forwarding. Such service counts as 10 words (e.g., a 25-word ad, plus a "Box Number", equals 35 words). All ads will be set in regular, uniform style, without display; the first word, only, in bold face type.

For display ads, using type larger or of a different style than the uniform settings, enclosed with separate border rules, the rate is \$16.00 per inch; no extra charge for "Box Numbers".

2. Advance Payment: All Personnel Placement ads, classified or display, must be accompanied by correct remittance, made payable to SCIENCE. Insertion can not be made until payment is received.

3. Closing Date: Advertisements must be received by SCIENCE, 1515 Mass. Ave., N.W., Washington 5, D. C., together with advance remittance, positively not later than 14 days preceding date of publication (Friday of every week).

POSITIONS WANTED

Academic chemical research appointment desired by young organic Ph.D. with six years industrial experience in pharmaceuticals and dyestuffs. Publications. Box 297, SCIENCE. X

Academic Position: M.S. Chemistry, physics, science, geology. Five years teaching, ten years industrial experience. Publications. N. M. Foote, Zelley Ave., Moorestown, N. J. X

Biologist; bacteriologist; graduate student; employed medical bacteriology; B.S. '48. Seeks industrial, medical position New York area. Box 293, SCIENCE. X

German, philosophy, European background, American citizen, Ph.D., over 50, interested in teacher training, will also consider administrative position. Box 295, SCIENCE. X

Horticulturist; B.S. (Agriculture), M.Sc., Ph.D., Horticulture; ten years' research and teaching; five years, superintendent, agricultural experiment station; for further information, please write Science Division, Medical Bureau (Burneice Larson, Director) Palmolive Building, Chicago. X

Plant Pathologist: Ph.D. September, 1950, with teaching and extension experience. Desires research or research-teaching position. Box 292, SCIENCE. X

Psychology, social, abnormal etc., man, Ph.D., very experienced, desires promotion. Box 294, SCIENCE. X

POSITIONS OPEN

Bacteriologist; B.S., Experienced research assistant for studies on chemotherapy of experimental tuberculosis. American Cyanamid Company, Stamford, Connecticut. 9/22

B.S. or M.S. or equivalent in biology or pre-medical courses for pharmacology laboratory of eastern pharmaceutical manufacturer. Must have definite interest in laboratory work and personality suited to close group activity. Give complete details including record of college courses taken and grades received. Box 296, SCIENCE. X

Positions Open:

(a) Associate medical director; large pharmaceutical company; duties administrative and clinical research; advantageous if Ph.D. in one of sciences; key appointment. (b) Physiologist with background of biochemistry and knowledge of aquatic invertebrates; work concerned with culturing of aquatic invertebrates, studying effects of various types of chemicals upon them; research institution. (c) Organic chemist; B.S. or M.S. degree required; research position, large industrial company; university medical center; Middle West. (d) Director of teaching program in experimental foods; strong background in organic and physical chemistry required; will consider Ph.D. in chemistry interested in working in Home Economics school; teaching experience essential; Middle Western college. (e) Ph.D. in biochemistry to assist in supervision of small chemistry department; part or full-time; medical student eligible; California. (f) Parasitologist to teach general zoology, parasitology, insect physiology and endocrinology; Middle Western college; immediately. S9-3 Science Division, Medical Bureau (Burneice Larson, Director) Palmolive Building, Chicago. X

Personnel Placement

PLACEMENT SERVICE IN ELECTRON MICROSCOPY

This Placement Service is maintained by the Electron Microscope Society of America to serve both employers and applicants.

- Applicants invited to send for data sheet to register
- Employers invited to send for form to list openings
- Applicants' data sheets sent to employers on request
- Available openings sent to qualified applicants on request
- No fee for this placement service to either party

ADDRESS:

Mr. M. C. Banca, Director
E.M.S.A. Placement Service
Parkview Apt.—419D
W. Collingswood 6, N. J.



**Electron Microscope
Society of America**

Are YOU seeking — new position ?
Your ad here will get RESULTS!

For "Charges & Requirements" see above

The Market Place

BOOKS

WANTED TO PURCHASE:
SCIENTIFIC PERIODICALS
Sets and runs, foreign and domestic
SCIENTIFIC BOOKS
Entire libraries and smaller collections
WALTER J. JOHNSON
125 East 23rd Street, New York 10, N. Y.

Send us your Lists of
SCIENTIFIC BOOKS AND PERIODICALS if
which you have for sale.
Complete libraries; sets and runs; and single titles are wanted.
Also please send us your want lists.
STECHERT-HAFNER, INC., 31 East 10th Street, New York 3.

Your sets and files of scientific journals
are needed by our library and institutional customers. Please send us lists and description of periodical files you are willing to sell at high market prices. J. S. CANNER AND COMPANY, 909 Boylston Street, Boston 15, Massachusetts. if

The Market Place

CHARGES and REQUIREMENTS for "MARKET PLACE" Ads

1. Rate: 20¢ per word for classified ads, minimum charge \$5.00 for each insertion. Such ads are set in uniform style, without display; the first word, only, in bold face type. For display ads, using type larger or of a different style than the uniform classified settings, and entirely enclosed with separate rules, rates are as follows:

Single insertion	\$16.00 per inch
7 times in 1 year	14.50 per inch
13 times in 1 year	13.00 per inch
26 times in 1 year	11.50 per inch
52 times in 1 year	10.00 per inch

2. Payment: For all classified ads, payment in advance is required, before insertion can be made. Such advance remittances must be made payable to SCIENCE, and forwarded with advertising "copy" instructions. For display advertisers, monthly invoices will be sent on a charge account basis—providing satisfactory credit is established.

3. Closing Date: Classified advertisements must be received by SCIENCE, 1515 Massachusetts Avenue, N.W., Washington 5, D. C., together with advance remittance, positively not later than 14 days preceding date of publication (Friday of every week).

For proof service on display ads complete "copy" instructions must reach the publication offices of SCIENCE, 1515 Massachusetts Avenue, N.W., Washington 5, D. C., not later than 4 weeks preceding date of publication.

LANGUAGES

LINGUAPHONE MAKES LANGUAGES EASY

At home learn to speak Spanish, Portuguese, Italian, French, German, Russian, by quick easy Linguaphone Conversational Method. Save time, work, money. Send for free book today. LINGUAPHONE INSTITUTE, 84-P Radio City, New York 20.

PROFESSIONAL SERVICES

SPECIAL GLASS APPARATUS

Our glass blowing department is available for special scientific and technical glass apparatus made to specifications and drawings. Inquiries invited. Estimates furnished.

E. MACHLETT & SON

218 East 23rd St. New York 10, N. Y.

Microbiologic Assay • Amino Acids

SHANKMAN LABORATORIES • Proteins

2023 S. Santa Fe, L. A. 21, Calif. • Vitamins

FOOD RESEARCH LABORATORIES, INC.

Founded 1922

Philip B. Hawk, Ph.D., President

Bernard L. Osier, Ph.D., Director

RESEARCH - ANALYSES - CONSULTATION

Biological, Nutritional, Toxicological Studies for the Food, Drug and Allied Industries

48-14 33rd Street, Long Island City 1, N. Y.

Write for descriptive brochure

TRANSLATIONS

... less than 1¢ a word—Write

READERS SERVICE • Box 4523, Washington 17, D. C.

The Market Place

PROFESSIONAL SERVICES



THE PANRAY CORP.

Research Division
340 CANAL ST., NEW YORK 13

- Microanalysis (C, H, N, S, Etc.)
- Custom Organic Syntheses
- Chemotherapeutics
- Sponsored Research

SUPPLIES AND EQUIPMENT

WEATHER INSTRUMENTS

Barometers • Thermometers • Psychrometers
Anemometers • Wind Vanes • Rain Gages

Send \$1.10 in stamps for catalog

SCIENCE ASSOCIATES

401 N. BROAD ST., PHILADELPHIA 6, PA.

White SWISS Mice 20c

Rabbits, Cavies, White Rats, Ducks, Pigeons, Hamsters

Write • J. E. STOCKER • Ramsey, N. J.

automatic Washers

for Pipettes • Animal Cages • Laboratory Glassware

Please state your requirements

HEINICKE Instrument Corp. • 315 Alexander St.
Rochester 4, N. Y.

STAINS

STARKMAN Biological Laboratory

• RARE
• COMMON
Price list on Request
• 461 Bloor St., W.
Toronto, Canada

ROGER® CAMERA TIMER

for time-lapse cinematography as used in many well-known institutions, here and abroad, for the study of slow processes. MICRO-CINEMA EQUIPMENT.

ROLAB Photo-Science Laboratories

SANDY HOOK, CONNECTICUT

* Formerly with Dr. Alexis Carrel.



GLYCOCYAMINE—Hydroxyproline, L-Methionine

- AMINO ACIDS • BIOCHEMICALS
- PRE-MIXED MICROBIOLOGICAL ASSAY MEDIA

H. M. CHEMICAL COMPANY, LTD.

144 North Hayworth Avenue Los Angeles 36, California

"Your animal is half the experiment"

SWISS ALBINO MICE

ALBINO - W RATS

**albino farms • P. O. BOX 331
RED BANK, N. J.**

The Market Place is continued on next page.

Enrich your
library with the
scientific and historic
value of this unique volume

Centennial



7½ x 10½ inches,
double column,
clothbound,
320 pages

Symposia presented
to commemorate the
first hundred years
of AAAS include
42 papers by lead-
ing scientists in thir-
teen major fields:

- Sciences of Society
- Educational Potentials
- Human Individuality
- Food and Nutrition
- Housing
- World Health Problems
- Sources of Energy
- The Upper Atmosphere
- The World's Natural Resources
- Genes and Cytoplasm
- High Polymers
- Interactions of Matter and Radiation
- Waves and Rhythms

- Cash price to AAAS members \$4.50
Nonmembers and institutions \$5.00

A.A.A.S. Publications
1515 Massachusetts Ave., N.W.
Washington 5, D. C.



Enclosed find my check or money order
in the amount of \$..... for
copy of *Centennial*.

NAME
ADDRESS
CITY ZONE STATE

ORDER NOW

The Market Place



Cargille MICRO BEAKERS

For direct weighing of small quantities of oils
(capacity 1 ML.) and fats for Iodine Number
Determinations (drop the glass beaker and sam-
ple into the solution).

For semi-micro procedures.

15 for \$1.00 Gross \$7.50
R. P. CARGILLE (DEPT. 5)
118 Liberty St. New York 6, N. Y.

LABORATORY ANIMALS

- Clean healthy well-fed animals
Guaranteed suitable for your needs.
Reasonably priced—Dependable service

DOGS RATS RABBITS
CATS PIGEONS HAMSTERS
MICE POULTRY GUINEA PIGS
JOHN C. LANDIS • Hagerstown, Md.

All Amino Acids (natural, synthetic, unnatural).
Rare Sugars, Biochemical Products, Reagents, New Pharma-
ceuticals in stock. Write or phone PLaza 7-8171 for complete
price list.

BIOS LABORATORIES, INC. 17 West 60th Street,
New York 23, N. Y.

a tested formula
for increasing your sales . . .

ADVERTISE in SCIENCE

Satisfied advertisers give proof that **SCIENCE**

• PRODUCES SALES

"Science is consistently our* most profit-
able medium. Business secured solely thru
SCIENCE ads has been the backbone of
our success in this field."

"... our client* joins us in expressing
our satisfaction at the results advertising
in **SCIENCE** has accomplished."

• INCREASES INQUIRIES

"The ——— Chemical Company* re-
ceived over 80 inquiries from a 1/4-page,
which was far more than they expected."

"**SCIENCE** is an exceptionally fine pro-
ducer of inquiries and sales for us."

• BUILDS DISTRIBUTION

"... we* feel that our advertisements in
SCIENCE have been of great value to us
in making our animals known throughout
the scientific world. . . . We consider it
one of the best mediums for this purpose."

* Names on Request

ATTENTION

**MANUFACTURERS
SERVICERS and
SUPPLIERS . . .**

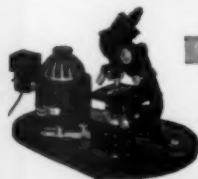
- Send your advertising copy NOW, for the October 6th
- Special **EQUIPMENT ISSUE**—featuring the latest develop-
ments in scientific equipment—which will be of direct interest
- to the more than 33,000 **SCIENCE** readers, especially those
- persons responsible for purchases by the country's leading
- educational institutions, industrial laboratories and research
- foundations. Regular rates apply—see pages 16 & 23.

for new horizons in Photomicrography & scientific photography the Orthophot



Designed for the ultimate in versatility, the new Silge & Kuhne Orthophot provides all the facilities for photomicrography (using any standard microscope), photomacrography, microprojection, photocopying, microfilming, x-ray copying, enlarging, and general laboratory and scientific photography.

Orthophot set up for photomicrography with standard microscope. Built-in, permanently-aligned light source with complete color and intensity controls. Precision reflex camera has split-micron focusing device.



MICROSCOPY

Separately, illustrated, or as part of complete Orthophot, Ortho-illuminator excels for routine microscopy, darkfield, and other research techniques, and particularly phase work. Near parallel beam of light, free from filament image, rises vertically from base, entering microscope condenser directly. Operation on a-c or d-c power.

Orthophot as shown at top (without microscope) \$825.00. f.o.b. destination U.S.A.



PHOTO-MACROGRAPHY

In seconds, Orthophot converts for photomacrography. Adjustable macro-stand replaces microscope. Same highly-controllable illumination and split-micron focusing used.



PHOTO REPRODUCTION

Black Bakelite table and oblique camera arm convert Orthophot to photocopy unit for gross specimens, drawings, photographs, papers, etc. Special table transilluminates.



ENLARGING

Substitution of enlarger head with opal-bulb light source and double condensing lens makes Orthophot into precision photoenlarger. Quick, needle-sharp focusing with illuminated target on table and using reflex mirror.



CINEMICROGRAPHY

Simplified column on Orthophot accommodates still cameras from miniatures to 4 by 5 Graflex types, almost all 8- and 16-mm cine cameras, and many 35-mm models. Extended adjustments provide alignment with standard microscopes.

Accessory units not shown include microprojection viewer with 8- by 8-in. vertical ground glass, alternative exposure meters approximately 20 and 2000 times as sensitive as standard commercial types, and bellows-extension adapters to increase magnification or establish fixed ratios.

This versatile equipment is supplied either in complete assemblies or in separate sections to coordinate with existing laboratory facilities. Write for descriptive data.

Silge & Kuhne

153 Kearny St. San Francisco 8, Calif.

Specialists in Microscopic and Photomicrographic Equipment

"Tailored" FOR TEACHING

— and LOWEST in Cost

Spencer Junior Stereoscopic Microscopes possess a unique combination of features valuable in classroom instruments. They are low in height and have slightly inclined eyepieces—as a result fatigue is reduced and students see clearly with comfort without straining necks and backs. Models with double revolving nosepieces require only a quick $\frac{1}{4}$ turn to switch from one power to another. Shielded by a circular housing, the paired objectives are completely protected from dust as well as abusive handling. Spencer Junior Stereoscopic Microscopes provide clear, erect images and wide, flat fields. Magnifications range from 6.8X to 98X. Priced well below other stereoscopic microscopes, they appeal to the school with a limited budget.



See your AO Spencer distributor for
a demonstration or write Dept. J3.

American  Optical
COMPANY
Instrument Division
Buffalo 15, New York

Makers of Microscopes for over 100 Years



